A.M.A.
Archives OF OPHTHALMOLOGY

MAY 1955
VOLUME 53 NUMBER 5

HEREDODEGENERATIONS AND HEREDOCONSTITUTIONAL DEFECTS OF RETINA — HERMAN ELWYN, M.D.

GAS GANGRENE PANOPHTHALMITIS — ROBERT B. LEAVELLE, M.D.

LEIOMYOMA OF THE IRIS — Lt. WAYNE L. ERDBRINK ET AL.

A TECHNIQUE FOR GONIOPHOTOGRAPHY — SEYMOUR GOODSTEIN, M.D., ET AL.

OCULAR EFFECTS PRODUCED BY HIGH-INTENSITY X-RADIATION — PAUL A. CIBIS, M.D., ET AL.

SCLERAL CHANGES INDUCED BY DIATHERMY IN RETINAL DETACHMENT — KENNETH C. SWAN, M.D., ET AL.

SYRINGOMA OF THE EYELIDS — L. EDWARD GAUL, M.D.

PHYSIOLOGICAL CHANGES IN CORNEA INDUCED BY CONTACT LENSES — GEORGE K. SMELSER, Ph.D., ET AL.

DEPENDENCE OF IOP-LOWERING EFFECT OF ACETAZOLEAMIDE ON SALT — V. EVERETT KINSEY, Ph.D., ET AL.

REDUCED OCULAR TENSION AFTER CATARACT SURGERY — A. C. HILDING, M.D., Ph.D.

THE FIELDS OF VISION AND THEIR SIGNIFICANCE WHEN PROJECTED INTO SPACE — H. S. WELSMAN, M.D., ET AL.

INTRAVENOUS TREATMENT OF OPTIC NEURITIS — PHILIP KAZDAN, M.D., ET AL.

A SIMPLE NOMOGRAM FOR PROBLEMS IN OPTICS — S. I. ASKOVITZ, M.D.

INCIDENCE OF COAGULASE-POSITIVE STAPHYLOCOCCI IN EXTERNAL OCULAR INFECTIONS — TED SUIE, Ph.D., ET AL.

LATE EFFECTS OF BETA RADIATION ON THE EYE — GEORGE R. MERRIAM JR., M.D.

EDROPHONIUM (TENSILON) IN DIAGNOSIS OF OCULAR MYASTHENIA GRAVIS — S. ARTHUR BORUCHOFF, M.D., ET AL.

COMPLETE CONTENTS ON FIRST PAGE

From Goodstein et al, p. 649

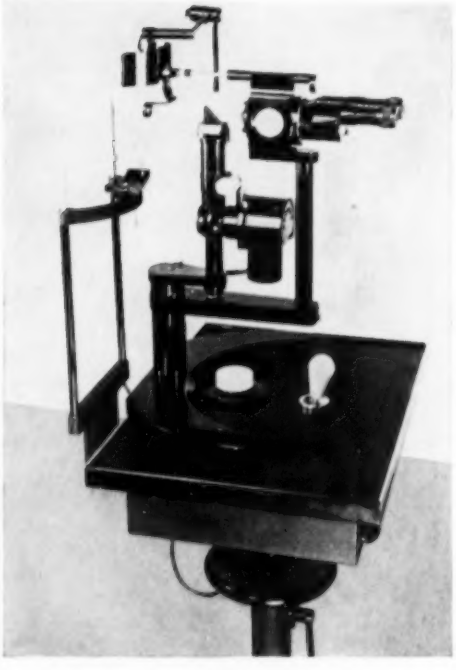
AMERICAN MEDICAL ASSOCIATION Publication

DOCTOR,

SEE IT IN OUR

INSTRUMENT DEPARTMENT—

the Zeiss Opton Slit Lamp



This slit lamp requires no adjustments whatsoever.

The slit lamp can be swung past the corneal microscope without interruption of observation.

The microscope can be set for five different magnifications solely by turning a knob without a change of oculars or objectives.

The working distance remains the same for all magnifications.

A supplementary attachment permits, in an optically correct and manually simple fashion, slit lamp microscopy of the deep vitreous—and binocular ophthalmoscopy in either white or red-free light.

All manipulative parts are positioned to facilitate quick and satisfying use of the instrument.

A fine optical instrument by Zeiss—a great name in optics.

Also available with compound stage to fit deluxe floor stand.

The House of Vision Inc.

30 NORTH MICHIGAN AVENUE, CHICAGO
MILWAUKEE • MINNEAPOLIS • DES MOINES

TABLE OF CONTENTS

VOLUME 53 MAY 1955 NUMBER 5

ORIGINAL ARTICLES

PAGE

Heredodegenerations and Heredoconstitutional Defects of Retina 619
Herman Elwyn, M.D., New York

Gas Gangrene Panophthalmitis 634
Robert B. Leavelle, M.D., North Hollywood, Calif.

Leiomyoma of the Iris 643
Lt. Wayne L. Erdbrink (MC), U. S. N., and Capt. Fred Harbert (MC), U. S. N. (Ret.)

A Technique for Goniophotography 649
Seymour Goodstein, M.D.; A. A. Cinotti, M.D.; Mortimer Cholst, M.D., and John P. Goeller, New York

Ocular Effects Produced by High-Intensity X-Radiation 651
Paul A. Cibis, M.D., St. Louis; Werner K. Noell, M.D., Buffalo, and Bertram Eichel, D.D.S., Randolph Field, Texas

Scleral Changes Induced by Diathermy in Retinal Detachment 664
Kenneth C. Swan, M.D., and Leonard Christensen, M.D., Portland, Ore.

Syringoma of the Eyelids 671
L. Edward Gaul, M.D., Evansville, Ind.

Physiological Changes in Cornea Induced by Contact Lenses 676
George K. Smelser, Ph.D., and D. K. Chen, B.S., New York

Dependence of IOP-Lowering Effect of Acetazoleaminde on Salt 680
V. Everett Kinsey, Ph.D.; Enriqueta Camacho, M.D.; Gerard A. Cavanaugh, M.S., Detroit; Marguerite Constant, St. Louis, and Daniel A. McGinty, Ph.D., Detroit, with the Technical Assistance of June B. Twomey, B.S.

Reduced Ocular Tension After Cataract Surgery 686
A. C. Hilding, M.D., Ph.D., Duluth, Minn.

The Fields of Vision and Their Significance When Projected into Space 694
H. S. Welsman, M.D., Guelph, Ont., Canada, and Clement McCulloch, M.D., Toronto, Canada

Intravenous Treatment of Optic Neuritis 700
Philip Kazdan, M.D., and Roscoe J. Kennedy, M.D., Cleveland

A Simple Nomogram for Problems in Optics 702
S. I. Askovitz, M.D., Philadelphia

Incidence of Coagulase-Positive Staphylococci in External Ocular Infections 706
Ted Suie, Ph.D., and Frank W. Taylor, M.D., Columbus, Ohio

Late Effects of Beta Radiation on the Eye 708
George R. Merriam Jr., M.D., New York

Edrophonium (Tensilon) in Diagnosis of Ocular Myasthenia Gravis 718
S. Arthur Borschoff, M.D., Boston, and Bernard Goldberg, M.D., New York

CLINICAL NOTES, NEW INSTRUMENTS AND TECHNIQUES

Fixation Forceps 720
Alfred A. Nisbet, M.D., San Antonio, Texas

REGISTRY OF INTERESTING CASES

Serum Sickness Manifested by Anterior Chamber Exudate 721
Mark Thumim, M.D., Middletown, Conn.

ANNUAL REVIEWS

Diseases of the Retina and Optic Nerve 722
Henry P. Wagener, M.D., Rochester, Minn.

SPECIAL REPORT

International Council of Ophthalmology and International Federation of Ophthalmological Societies 755

CORRESPONDENCE

Balint's Syndrome and Ocular Motor Apraxia 758
David G. Cogan, M.D., and Raymond D. Adams, M.D., Boston

REGULAR DEPARTMENTS

News and Comment 642, 720, 721, 759
Books 763

A. M. A.
ARCHIVES OF OPHTHALMOLOGY

VOLUME 53 MAY 1955 NUMBER 5

COPYRIGHT, 1955, BY THE AMERICAN MEDICAL ASSOCIATION

Continuing the Publication

FOUNDED BY HERMAN KNAPP, 1869

EDITORIAL BOARD

FRANCIS HEED ADLER, Chief Editor

313 South Seventeenth Street, Philadelphia 3

WILLIAM ZENTMAYER, Philadelphia

W. L. BENEDICT, Rochester, Minn.

KENNETH C. SWAN, Portland, Ore.

WILLIAM F. HUGHES Jr., Chicago

DAVID G. COGAN, Boston

JONAS S. FRIEDENWALD, Baltimore

JOHN H. DUNNINGTON, New York

ASSOCIATES:

Alson E. Braley

F. Phinizy Calhoun Jr.

A. Gerard DeVoe

Trygve Gundersen

Joseph S. Haas

John E. Harris

John M. McLean

Paul W. Miles

Frank Payne

Ludwig von Sallmann

Henry P. Wagener

Maynard C. Wheeler

AUSTIN SMITH, Editor, A. M. A. Scientific Publications

GILBERT S. COOPER, Managing Editor, Specialty Journals

AMERICAN MEDICAL ASSOCIATION
Scientific Publications

The Journal of the American Medical Association. Weekly. Annual Subscription Price, $15.00.

Quarterly Cumulative Index Medicus. Issued Twice a Year. Subscription Price, Calendar year, $20.00.

A. M. A. Specialty Journals
Monthly

A. M. A. Archives of Internal Medicine. Paul S. Rhoads, M.D., Chief Editor, American Medical Association, 535 N. Dearborn St., Chicago 10. Price, $10.00; Canada, $10.50; Foreign, $11.50; individual copy, $1.00.

A. M. A. Archives of Dermatology. Paul A. O'Leary, M.D., Chief Editor, 200 First St. S.W., Rochester, Minn. Price, $12.00; Canada, $12.50; Foreign, $13.50; individual copy, $1.25.

A. M. A. Archives of Ophthalmology. Francis Heed Adler, M.D., Chief Editor, 313 S. 17th St., Philadelphia 3, Price, $12.00; Canada, $12.50; Foreign, $13.50; individual copy, $1.25.

A. M. A. Archives of Surgery. Waltman Walters, M.D., Chief Editor, American Medical Association, 535 N. Dearborn St., Chicago 10. Price, $14.00; Canada, $14.50; Foreign, $15.50; individual copy, $1.25.

A. M. A. American Journal of Diseases of Children. Robert Barrett Lawson, M.D., Chief Editor, 1000 N.W. 17th St., Miami 36, Fla. Price, $12.00; Canada, $12.50; Foreign, $13.50; individual copy, $1.25.

A. M. A. Archives of Pathology. Paul R. Cannon, M.D., Chief Editor, Department of Pathology, University of Chicago, The School of Medicine, 950 E. 59th St., Chicago 37. Price, $8.00; Canada, $8.50; Foreign, $9.25; individual copy, $1.00.

A. M. A. Archives of Neurology and Psychiatry. Tracy J. Putnam, M.D., Chief Editor, 450 N. Bedford Drive, Beverly Hills, Calif. Price, $12.00; Canada, $12.50; Foreign, $13.50; individual copy, $1.25.

A. M. A. Archives of Otolaryngology. George M. Coates, M.D., Chief Editor, 1721 Pine St., Philadelphia 3. Price, $12.00; Canada, $12.50; Foreign, $13.50; individual copy, $1.25.

A. M. A. Archives of Industrial Health. Prof. Philip Drinker, Chief Editor, Dept. of Industrial Hygiene, Harvard University School of Public Health, 55 Shattuck St., Boston 15. Price, $8.00; Canada, $8.50; Foreign, $9.00; individual copy, $1.00.

Check, money orders, and drafts should be made payable to the American Medical Association, 535 North Dearborn Street, Chicago 10.

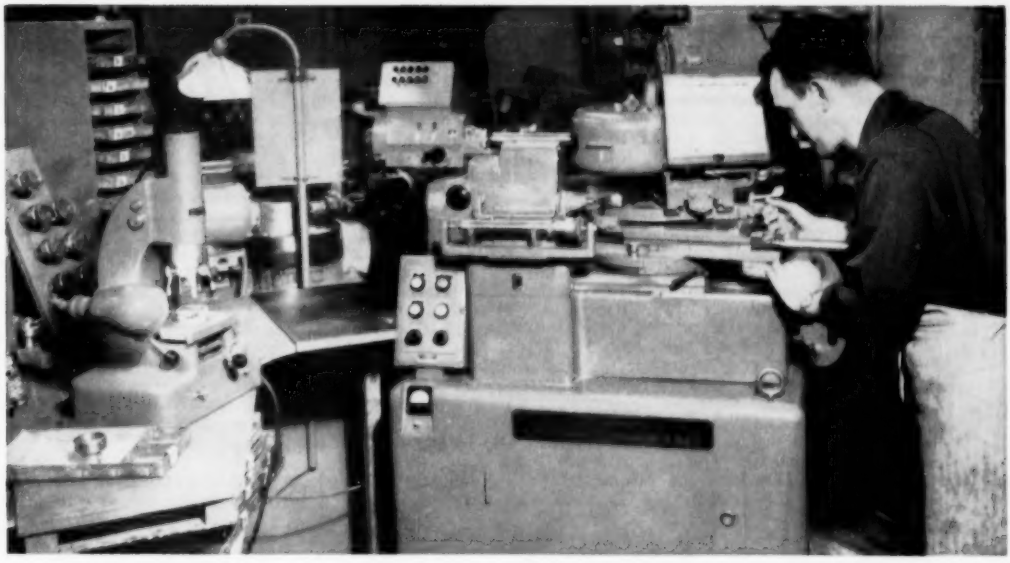
Published Monthly by

AMERICAN MEDICAL ASSOCIATION

535 NORTH DEARBORN STREET • CHICAGO 10, ILLINOIS

Entered as Second Class Matter Feb. 7, 1929, at the Postoffice at Chicago, Under the Act of March 3, 1879. Annual Subscription, $12.00

Here, in Benson's Laboratories, you'll find...



Men and Machines

In manufacturing optical products which *must* be precise, the skill of master craftsmen is essential. Add to that skill the most modern production equipment and you have a combination unsurpassed.

Forty-two years of continuous growth have produced BENSON branches in 27 cities of the Upper Midwest . . . laboratories where prescriptions are *accurately* transformed into fashionable glasses.

And the "BENSON" name has come to stand for the highest quality and precision in optical production.

May we serve you?

Since 1913 **Benson** OPTICAL COMPANY *Executive Offices • Minneapolis, Minn.*

COMPLETE LABORATORIES CONVENIENTLY LOCATED IN LEADING UPPER MIDWEST CITIES

Instructions to Contributors

Communications regarding editorial management, subscriptions, reprints, etc., should be addressed to Specialty Journals, American Medical Association, 535 North Dearborn Street, Chicago 10.

Articles, book reviews, and other materials for publication should be addressed to the Chief Editor of the Specialty Journal concerned. Articles are accepted for publication on condition that they are contributed solely to that journal.

An original typescript and the first carbon of an article should be provided; it must be double or triple spaced on one side of a standard size page, with at least a 1-inch margin at each edge. An article in English by a foreign author should be accompanied by a draft in the author's mother tongue. Improvised abbreviations should be avoided.

The main title of an article may not contain more than ninety characters and spaces; a subtitle may be of any length. The subtitle should be sufficiently detached from the main title that a punctuation mark as strong as a colon can be used in the Table of Contents to separate it from the main title; it must not begin with "with."

The author's name should be accompanied by the highest academic or medical degree which he holds. If academic connections are given for one author of an article, such connections must be given for all other authors of the article who have such connections.

Typographic considerations necessitate that the first paragraph of an article contain not fewer than thirty words. A Case Report must be preceded by an introductory paragraph containing at least thirty words before the details of the case are given.

Material quoted from another publication must be quoted exactly if the original is in English—spelling, capitalization, punctuation, etc., unchanged. Material taken largely from another publication must be credited to the original author, whether quoted exactly or merely abstracted. If such material is quoted indirectly, the author must be careful to leave no complete sentence of the original unaltered. Use of uncredited quotations will be sufficient cause for rejection of an article.

Each article should be accompanied by a summary in the present tense, presenting the main points of the article, but in somewhat more generalized terms than in the article itself.

If it is necessary to publish a recognizable photograph of a person, the photograph must be accompanied by written permission of the subject himself if an adult, or of the parents or guardian if a child, to publish his photograph. An illustration which has been published in another publication must be accompanied by written permission from the author and the original publisher to reproduce it in an A. M. A. Specialty Journal.

The maximum illustration allowance is ten illustrations within a total of 100 sq. inches or $100, whichever is of greater advantage to the author. When no restrictions are placed by the author upon cropping, reducing, and grouping, the publisher is often able to use twenty or more illustrations in one article within the $100 allowance. Submit sharp prints of the following sizes, 2½″ wide × 2½″ or 3½″ high, 3½″ wide × 2½″ high, and 5½″ or 7″ wide × 3½″ high, to minimize reduction and/or cropping. Oversized originals should be photographed and a print submitted. Large photomicrograph prints will be reduced in scale unless portions to be cropped are indicated by the author.

Any cut-off marks should be made on the margins or mountings rather than on the illustration itself. Charts and drawings should be in black ink on hard, white paper. Lettering must be large enough to permit necessary reduction. Glossy prints of x-rays are requested. Paper clips should not be used on prints, since their mark shows in reproduction, as does writing on the back of prints with hard lead pencil or stiff pen. Labels should be prepared and pasted to the back of each illustration showing its number, the author's name, an abbreviated title of the article, and top plainly indicated. Charts and illustrations must have descriptive legends, grouped on a separate sheet. Tables must have captions. IT IS PREFERRED THAT ILLUSTRATIONS BE UNMOUNTED.

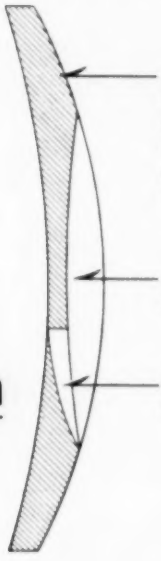
References to the literature should be numbered in the order in which they are referred to in the text or listed in alphabetical order without numbers. A chronological arrangement, with all entries for a given year alphabetized according to the surname of the first author, may be used if preferred. References should be typed on a special page at end of manuscript. They should conform to the style of the Quarterly Cumulative Index Medicus, and must include, in the order given, name of author, title of article (with subtitle), name of periodical, with volume, page, month—day of month if weekly or biweekly—and year. Names of periodicals should be given in full or abbreviated exactly as in the Quarterly Cumulative Index Medicus. Reference to books must contain, in the order given, name of author, title of book, city of publication, name of publisher, and year of publication. Titles of foreign articles, if originally in a generally known Romance or Germanic tongue, must either all be in English translation or all be in the original language. Titles in other languages must be translated. The author must assume responsibility for the accuracy of foreign titles.

Matter appearing in the A. M. A. Specialty Journals is covered by copyright, but as a rule no objection will be made to its reproduction in a reputable medical journal if proper credit is given. However, the reproduction for commercial purposes of articles appearing in the A. M. A. Specialty Journals, or in any other publications issued by the Association, will not be permitted.

AMERICAN MEDICAL ASSOCIATION

535 North Dearborn Street **Chicago 10**

As good
to look **at**
as it is good to
look **through**


Major Lens: Special Nokrome Crown glass. (Plus-power in the lenticular edge, though much weaker, allows patient some recognition of form in peripheral vision.)
Lenticular Field: Special high index barium glass.
Bifocal Segment: Same high index glass as lenticular field.

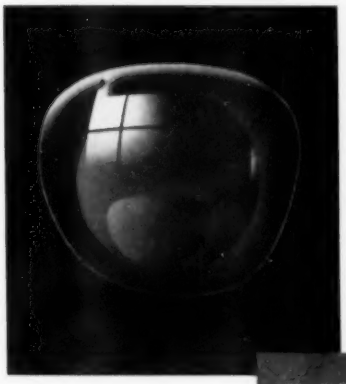
Fused Lenticular Panoptik Cataract Bifocal

Here's the lens to provide the greatest possible satisfaction to aphakic patients. It's lighter in weight, thinner—usually more than one third thinner than a one-piece bifocal of the same power—and has flatter front curves.

The Panoptik segment shape is ideally suited to the cataract patient. It offers a wide reading field at normal reading level. Flexibility, too, in base curves—bi-convex, plano base or −3.00 base—can be produced from the same blank. This facilitates service from the laboratory—a single pair of blanks, in each of the called-for reading additions, constitutes a stock from which any aphakic prescription can be made.

From both standpoints—cosmetic appearance and optical performance—the Panoptik Lenticular Cataract bifocal sets the standard of excellence.

In Soft-Lite, too



BAUSCH & LOMB
SINCE 1853

BVI

BVI CAMPAIGN ROLLING IN HIGH!

Backbone effort will be powerful, opinion-moulding full pages in the Saturday Evening Post and Vogue.

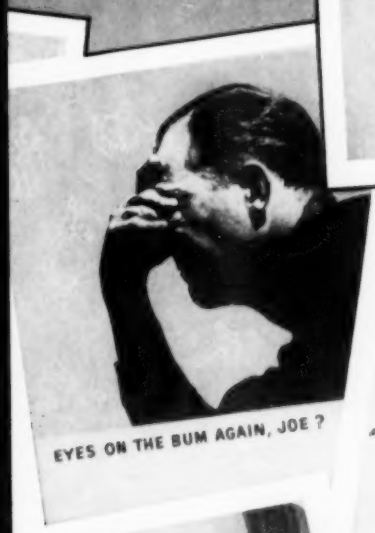
Major theme is eye care, supplemented by eye wear fashions. A minimum of 165 million reader-impressions are possible in this hard-hitting, month-after-month educational drive to put eye care and eye wear in the *public eye*.

Supporting campaigns in television, motion pictures, radio and literature will add additional millions of impressions. With industry-wide support, the months and years ahead look bright for all in eye work.

Better Vision Institute, Inc. 630 Fifth Avenue, New York 20, N. Y.

Seeing Fashion...
FOR MR. McWISE, 3 PAIRS OF EYES!
Split-second decision
that calls for Eagle-
For the hardest job in the world...
good vision is a must
4 KEYS TO Eye Beauty!

BVI

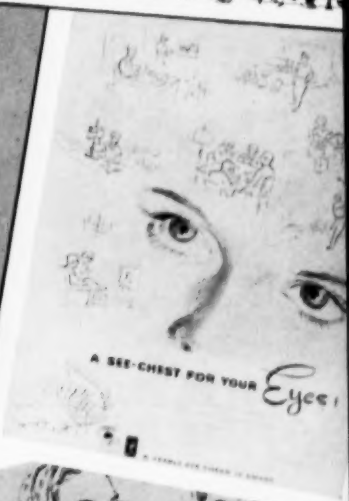


EYES ON THE BUM AGAIN, JOE?

EYE FASHION IS HIGH FASHION

Now is the time to have your vision checked!

ARE YOUR GLASSES DATED?



A SEE-CHEST FOR YOUR Eyes!

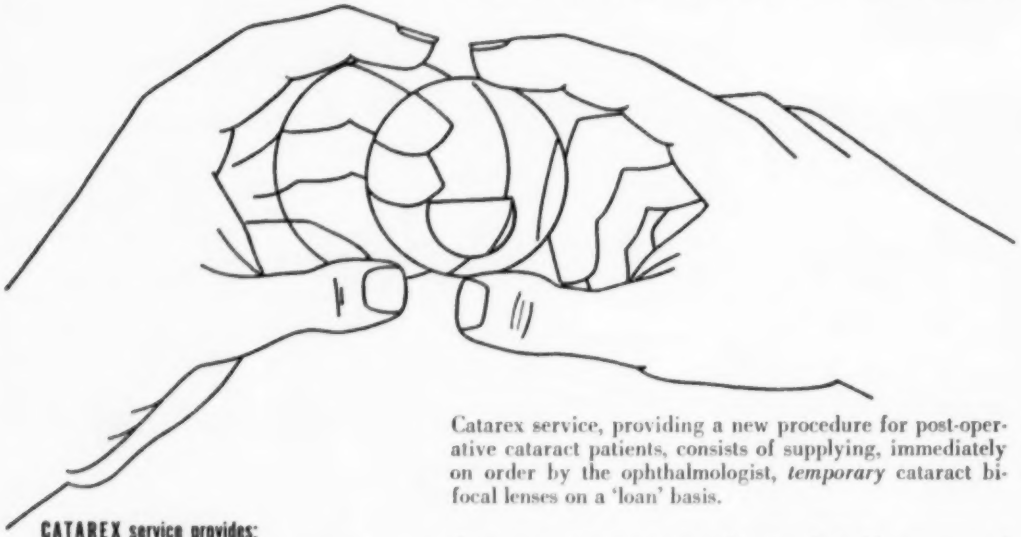
DOES TV PUT YOUR EYES ON THE BLINK?

His poor report card may be YOUR failure

The Big Giveaway...

after cataract surgery..... CATARX EX

THE TENTATIVE Rx FOR APHAKIC CASES



CATAREX service provides:

- *a succession of temporary adjustment lenses of the necessary power to temper the shock of transition to complete aphakic correction*
- *immediate, accurate correction in sphere, cylinder and axis in a lightweight, cosmetically excellent lens in a modern straight-top bifocal*
- *the necessary lens changes as ordered by the ophthalmologist*
- *a simple method of determining the most accurate Rx, including comfortable pupillary distance, bifocal segment height and position*
- *elimination of vertex distance measurements*
- *doing away completely with the unhappy requirement of resurfacing and replacement of permanent lenses during the adjustment period*
- *an identical PERMANENT bifocal, Vision-Ease Catarex 'D', for the final Rx*

Catarex service, providing a new procedure for post-operative cataract patients, consists of supplying, immediately on order by the ophthalmologist, *temporary* cataract bifocal lenses on a 'loan' basis.

Catarex service makes possible the desirable measure of fitting aphakic individuals *earlier* in the post-operative course, with a minimum of transition shock. There is no need for expensive, and sometimes unsatisfactory, resurfacing of permanent lenses due to changes in the Rx during the transition period. The prescription may be changed quickly, easily and inexpensively as many times as necessary, in order to arrive at the proper final correction.

In actual clinical practice, more than *96% of all cataract Rxes* have been satisfactorily completed by the use of Catarex lens service and the prescribing of Catarex 'D' cataract bifocals in the final Rx.

Ask your optician or optical laboratory about Catarex service.

THE

VISION-EASE

CORPORATION

Saint Cloud, Minnesota

See . . .

Mansfram

WITH *BARRELOC

in the new

DUSK GRAY

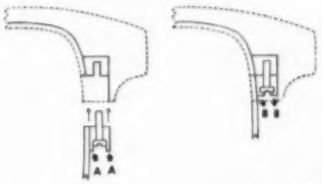
Combined with

1/10 12K white Rhodium

plated gold filled

*PAT. PENDING

BARRELOC



EARS OPEN EARS CLOSED

HOW IT WORKS: Insert eyewire screw in barrel and tighten in usual manner. *Sketch at AA shows screw in barrel with "ears" open.* Then with screwdriver, simply turn down the two ears over the screw head, as shown at BB. *The screw is locked in, can't back out.* For lens replacement, simply bend the ears back and unscrew as usual.

DUSK GRAY is a soft, dark, rich shade, subdued enough to suit masculine taste. As in a top grade gray flannel, faint traces of lighter gray enliven the tone. Add MANSFRAM in DUSK GRAY to your stock or samples. It's a coming color.

And remember, the most important screw in a spectacle frame is a loose screw and loose screws don't happen on the MANSFRAM with BARRELOC.

OTHER MANSFRAM COLORS: *Cordovan and Mello, Ebony and White.*

Continental INDIANAPOLIS

The Purpose of the Guild

- The aim of the Guild of Prescription Opticians of America is to advance the science of ophthalmic optics through the development of a country-wide ethical optical dispensing service that comprehensively meets the needs of the Eye Physicians and their patients; and to educate the public to the fact that the Eye Physician-Guild Optician type of eye service truly renders the most desirable form of eye care.

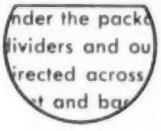
This statement of the Guild's purpose is reprinted from the cover of the REFERENCE LIST OF GUILD OPTICIANS, a geographical index of all our members. If you would like a copy, just drop a two-penny post card to

The Guild of Prescription Opticians of America, Inc.
110 E. 23rd Street New York (10) N.Y.

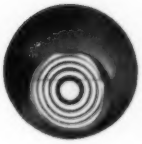
• UNIVIS B • UNIVIS R • UNIVIS D-28 • UNIVIS CV-6 • NU

• LINE 7 CV • VOCATIONAL CV • SINGLE VISION CATARACT • "D" SEG CATARACT •

• D SIAINU • TRIFOKAT • BIFOKAT • LENTICULAR "D" • LENTICULAR "T" • DOUBLE D •

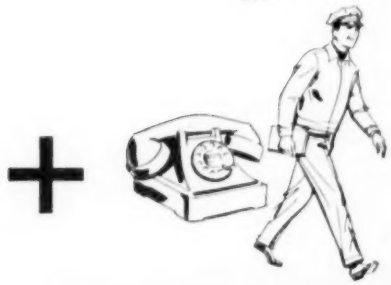


design and performance



manufacturing quality

patient acceptance



service

put them all together, they spell

Univis D
CORRECTED CURVE LENSES

Superior design? Superior performance? Ask the imitators! But the Univis quality standards which contribute so much to patients' satisfaction with your Rx can't be imitated. Quickly available from the nation's top laboratories.

THE Univis LENS COMPANY • Dayton, Ohio • New York, Chicago, Los Angeles, San Francisco

UNIVIS

COMMAND PERFORMANCE FRAMES • MASCULON • ENSEMBLE

KONO BASIC PROGRAM

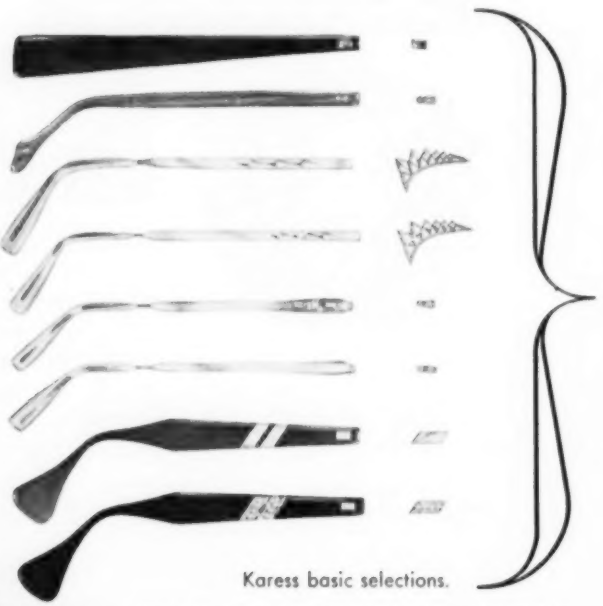
time to expand...

WITH KONO 'ROUND THE CLOCK!

- **You take a basic front...**
- **Pair it with any combination of temples and trims...**

And Presto!...you've just increased your frame potential to a versatile selection that expands according to your patients' needs! Now you have an infinitely wide range of styles to offer...because with kbp you can "custom-style" any frame to fit a specific need...merely by switching temples and trims. Truly a dawn-to-dark frame presentation to please every whim!

And best of all, your Kono distributor is solidly behind kbp. He's completely equipped with basic sparkling Konoptic fronts, temples and trims...diversified selections to service you quickly, efficiently, neatly.



Karess basic selections.

Contact your local supply house for further information.

NOBEL—Crisply styled for smart looks, superb fit.

KARESS—A basically youthful frame for every facial type.

KONETTE—A perennial favorite no matter what the occasion!

DARCY—The graceful costume frame so many women ask for.

NOBEL JR. & MISS KAY—A youth-loving pair youngsters really go for!

the KONO Kono manufacturing company

69-24 FORTY-NINTH AVENUE, WOODSIDE, N. Y.

LOS ANGELES, CALIF. • CHICAGO, ILL. • ATLANTA, GA. • CHARLESTON, S. C. • COLUMBUS, O.

eye dressings are neater, cleaner with

TUCK CELLOPHANE TAPE

You can provide additional comfort and efficiency by using Tuck Cellophane Tape for holding eye dressings in place.

Adhesion of Tuck Cellophane Tape to the skin is constant for a long period of time. It is notably free from irritation. There is no accumulation of dust or dirt to the surface so that the clean natural appearance of the transparent cellophane remains unchanged. Frequent washings of the surrounding areas will not affect the adhesion.

Tuck Cellophane Tapes can be removed quickly and with minimum irritation of the facial hair and skin.

SPECIAL INTRODUCTORY OFFER

With your order for 12 rolls of half-inch wide tape (2592 inches long) at $1.15 per roll, you will receive, without extra charge, a handsome desk-size tape dispenser — worth $2.95 — to facilitate faster and easier application.

Please add 50c for postage

WORLD TRADE CO.
100 EMERSON PLACE
BROOKLYN 5, N. Y.

Attached is my check for $14.30. Please send me 12 rolls of half-inch Tuck Cellophane Tape and free desk model dispenser.

NAME .....

ADDRESS .....

CITY .....

STATE .....

In N. Y. C., please add 3% sales tax

Most modern offices and factories are equipped with the best in scientific lighting facilities—but, they reflect on surfaces of glasses. These "GHOST" reflections are annoying and contribute to fatigue. MAY-O-LITE coated lenses can help eliminate these annoyances.

Complete Your Professional Service By Adding

The Best in Sight
MAY-O-LITE
Low Reflection Coating

MAY RESEARCH, INC., Box 1181, Minneapolis 1, Minn.

New Glover FRAMETAINER

exclusive in Glover FRAME CABINETS

Classifies 144, 96 or 48 frames at your fingertips.

We're glad to send you complete information on the items checked.

- ☐ **Glover FRAME CABINETS**
- ☐ **Glover FITTING DESKS**
- ☐ **Glover FRAME PANELS and TILES for office wall frame presentation.**
- ☐ **Glover Plan for Correlated Frame Dispensing.**

Recommended by your optical supply house.

GLOVER PRODUCT

P. O. BOX 4093
AUSTIN 51, TEXAS

LEADING DESIGNER AND MANUFACTURER OF OPTICAL FRAME DISPENSING EQUIPMENT SINCE 1951.

Copyright 1955 by A. D. Glover

One finger selection for all 3

dioptric lens
aperture
light intensity

with the 40
National Ophthalmoscope

This is one of the most compact, light and easily handled instruments of its kind. Operator can, with one finger, *without changing the original examining position:* select dioptric lens . . . select aperture . . . control light intensity. No fuss, no elaborate adjustment. In addition to simple functional efficiency, it offers reliability at moderate cost.

Has dioptric range of −20 to +25 . . . 4 apertures for: standard, pin-hole, vertical slit illumination and red-free filter . . . built-in fixed focus double condensing lens . . . magnified illuminated numerals . . . dust-proofed . . . durably finished, matt black . . . supplied with large or medium battery handle.

National

It's Lifetime

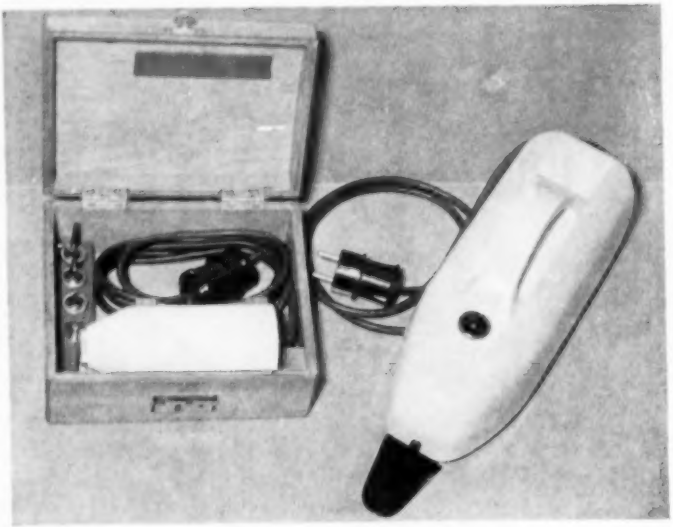
Guaranteed!

ASK YOUR DEALER TO SHOW YOU . . . 40 and 2340

NATIONAL ELECTRIC INSTRUMENT CO., INC.,
ELMHURST 73, N. Y.

storz
Surgical Instruments

NEW • LIGHT • POWERFUL



STORZ ATLAS **Hand Eye Magnet**

E-6650—Eye Magnet, Atlas: complete with four tips in wooden case and separate rectifier with footswitch. Small size for maneuverability and ease of handling. The magnet weighs 4.6 lbs. The rectifier with footswitch weighs 8.7 lbs. The type of tip selected is dependent on the position of the splinter. For strongest pulling power, the large cone tip is applied. More effective results are obtained by stepping on the footswitch repeatedly to get short interrupted pull rather than a long steady pull.

Power: The strong pulling power is similar to that given by the giant magnet. The absolute pulling power at the flange is 12.5 kg. or 28 lb. The ball jump power is 38.5 mm. The handling is not interfered with by strong directional pulls.

Advantages...

Small size—*maneuverability*
Light weight—*easily handled*
Versatile—*selection of tips*
POWER! — POWER! — POWER!

Made for 110 volt, 60 cycle, alternating current. If other current or voltage is desired, please specify. Uses 150 watts.

Developed and tested at the University Eye Clinic in Kiel.

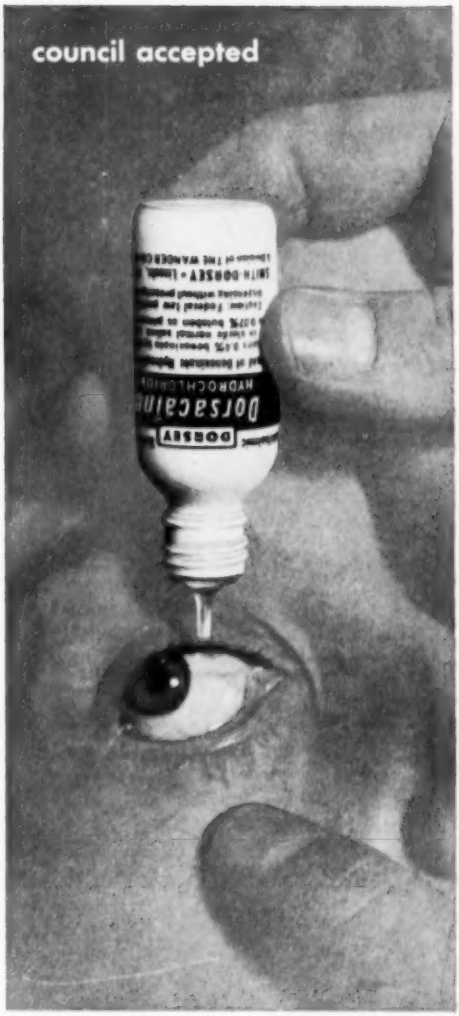
Complete—$149.50

Storz Instruments are available from Storz salesmen only. We do not distribute under any other name or trademark.

Order directly from

Storz Instrument Company

4570 Audubon Ave. **St. Louis 10, Mo.**



new corneal anesthetic

rapid action and

short duration*

virtually **nonsensitizing**
no cases reported of dermatitis occurring in patient's eye or on hands of physician.

relatively **nonirritating**
does not sting or burn when dropped into the eye—changes in the corneal epithelium or hyperemia of the conjunctiva rarely occur.

Average dose: *for tonometry,* 2 drops. *For minor surgical procedures,* 2 drops instilled 3 times at 90 second intervals.

Supplied: sterile normal saline solution with 0.02% Butoben as preservative, and containing 0.4% Dorsacaine Hydrochloride (benoxinate hydrochloride). In ½ oz. plastic squeeze bottle with dropper tip which delivers uniform drops (approximately 45 drops per cc.).

*Schlegel, H. E., Jr., and Swan, K. C.: A. M. A. Arch. Ophth. *51*:663 (May) 1954.

DORSACAINE®

HYDROCHLORIDE

SMITH-DORSEY • Lincoln, Nebraska • A Division of The Wander Company

Complete ARTIFICIAL EYE *Service*

Experience gained through over 100 years of artificial eyemaking enables us to produce and fit the very finest in artificial eyes. Glass and plastic eyes made to order or available from stock. Eyes fitted to all types of motility implants

artificial eye selection through the mail

Orders filled the same day received
Eyes sent on memorandum
Liberal assortment of either glass or plastic
Samples accurately matched
Superior quality eyes—Finest workmanship

WRITE FOR FREE COLOR CHART AND SIZE GUIDE

Serving the Profession Since 1851

Mager and Gougelman, inc.

30 NORTH MICHIGAN AVENUE • CHICAGO 2, ILLINOIS

DETROIT • CLEVELAND • KANSAS CITY • MINNEAPOLIS • NEW ORLEANS • ST. LOUIS
NEW YORK • BOSTON • BUFFALO • PHILADELPHIA • PITTSBURGH • WASHINGTON

"LACRILENS"®

is a safe lens

The test of time proves that the "LACRILENS"® contact lens can be worn for long periods of time in aphakia and in all sports, including swimming. *Write For Brochure*

Obrig Laboratories Inc.

49 East 51st Street, New York 22, N. Y.

Manufacturers of all types of Contact Lenses

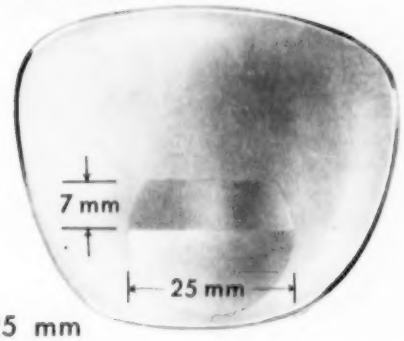
Branches in
PHILADELPHIA • MONTREAL • JOHANNESBURG

NOT TOO LARGE . . . NOT TOO SMALL . . .

Just Right . . .

for most

Rx needs!



TITMUS 7/25 mm

STRAIGHT TOP TRIFOCALS

Made for the average presbyope, the 25 mm width and the 7 mm intermediate provide a comfortably wide reading field, while the straight top design permits the greatest possible use of the distance correction. Not too large; not too small—but just right for patient satisfaction! A regular stock multifocal—available from your Titmus Independent Distributor.

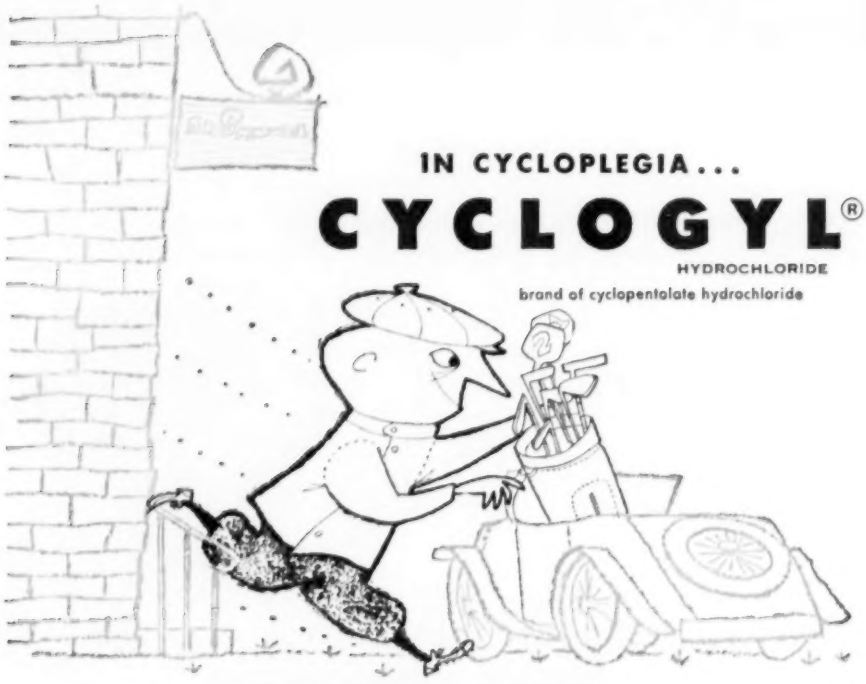
In White, Velvet-Lite A and B

OTHER TITMUS STRAIGHT TOP TRIFOCALS:

6/22 7/22 8/22 7/25 6/28 7/28 8/28

Titmus **OPTICAL COMPANY, INC.**

Manufacturers of Ophthalmic Lenses, Frames, Sun Glasses • Petersburg, Virginia



IN CYCLOPLEGIA . . .

CYCLOGYL®

HYDROCHLORIDE

brand of cyclopentolate hydrochloride

SAVES TIME

. . . for you . . . with rapid onset of action

. . . for your patients . . . with rapid recovery

"Cyclopentolate hydrochloride . . . produces a rapid [30 to 60 minutes], intense cycloplegia and mydriasis of moderate duration . . . and is effective in highly pigmented irises and for persons of all ages." *New and Nonofficial Remedies, Philadelphia, J. B. Lippincott Company, 1954, p. 189.*

Cyclogyl has shown outstanding qualities in 1035 cases.[1]
(Incorporates work of 11 previous investigators)

Compound	Dosage and Administration (drops) *	Diopters of Residual Accommodation	Spontaneous Recovery (in hr.)
Cyclogyl 0.5%	2	1.10	24†
Homatropine 2% or 4%	2	2.00	48

*Successive drops at five-minute intervals.

†Recovery time reduced to six hours after one percent pilocarpine.

1. *Gordon, D. M., and Ehrenberg, M. H.: Am. J. Ophth. 38:831 (Dec.) 1954.*

"the chief handicap of maximum cycloplegia, namely its incapacitating effect, is minimized . . ." *Getter, B. C.: A.M.A. Arch. Ophth. 51:467 (Apr.) 1954.*

Cyclogyl, "by virtue of its brevity, rapidity of action, and consistent depth of cycloplegia, will be [a drug of choice] for routine refraction . . ." *Ehrlich, L. H.: New York J. Med. 53:3015 (Dec. 15) 1953.*

Dosage:

Cycloplegia — One drop 1.0%, in each eye (or two drops of 0.5%) produces maximal cycloplegia in 30-60 minutes. Recovery time is normally 4-12 hours spontaneously. Pilocarpine reduces recovery time. In deeply pigmented eyes, 2 drops of 1.0% in each eye, instilled 10 minutes apart, achieves satisfactory cycloplegia in 98% of cases.

Mydriasis — One or two drops of 0.5% in each eye.

Samples and Literature on request.

Supplied:

Sterile ophthalmic solution in Gifford's Buffer (pH 6.0)
0.5% Solution — 15 cc Dropper Bottles
1.0% Solution — 15 cc Dropper Bottles
2 cc Dropper Bottles

Schieffelin & Co. Since 1794

Pharmaceutical and Research Laboratories
New York 3, N. Y.

Heredodegenerations and Heredoconstitutional Defects of the Retina

HERMAN ELWYN, M.D., New York

CONTENTS

Heredodegenerations Involving the Elastic Layer of Bruch's Membrane
- Kuhnt-Junius Disciform Macular Degeneration
- Angioid Streaks
- Cases of Sorsby and Mason

Heredodegenerations of the Neuroepithelium
- Heredodegeneration of the Macula Lutea
- Primary Pigmentary Degeneration of the Retina
- Laurence-Moon-Biedl Syndrome
- Gyrate Atrophy of the Choroid and the Retina
- Choroideremia

Heredoconstitutional Defects of the Neuroepithelium
- Congenital Night Blindness Without Fundus Changes
- Oguchi's Disease: Congenital Night Blindness with Grayish-White Discoloration of the Fundus
- Retinitis Punctata Albescens

Heredodegeneration of the Inner Nuclear Layer
- Cystoid Degeneration of the Retina
- Retinitis Circinata

Heredodegeneration of the Ganglion Cells of the Retina
- Infantile Amaurotic Family Idiocy, or Tay-Sachs Disease
- Juvenile Amaurotic Family Idiocy (Vogt-Spielmeyer or Stock-Spielmeyer Type)
- Late Infantile Amaurotic Family Idiocy (Bielschowsky, or Batten-Mayou Type)
- Niemann-Pick Disease

INTRODUCTION

Degenerations of the retina on a hereditary basis present a variety of problems (1) as to the character of the hereditary factors, (2) as to the ultimate factors in the pathogenesis, and (3) as to the autonomy of the individual clinical syndromes. The following discussion is an attempt to delimit the individual heredodegenerative entities pathologically and clinically. As a preliminary to such a discussion, it is necessary to define the terms used.

I

By degeneration on a hereditary basis, or heredodegeneration, I mean the gradual disappearance of certain cells or tissues without any apparent cause; the premature death of certain cells or tissues, for which Gowers introduced the term abiotrophy. It is assumed at the present time that for each of the metabolic activities of the cell there is an enzymatic system there, and that for each of these systems there is a gene. In the concept of heredodegeneration there is the implication that the genes which have to do with the enzymatic activities of certain cells are defective. The genes exert their activities for a variable period of time, in years, but there comes a time when they gradually cease their control. The result is the gradual reduction in the activities of the specific enzymatic systems within the cell with eventual death of the cell. Such a degeneration and eventual death of cells may occur at any time, although the cells were healthy at birth. The loss of the cells expresses itself in the loss of their function. Of the fundamental change in the genes nothing is known.

There is another way by which degeneration and eventual death of functional cells are brought about. In certain cells there accumulates a metabolic substance which the cell is not able to utilize. The basic functional activities of the cell are not disturbed for some time. Eventually, the increasing accumulation of an unutilizable substance interferes with its basic activities and the cell degenerates and dies. The inability to utilize a metabolic substance on the part of the cell

must necessarily be of genetic origin, with some inherent defect in the genes. Some heredodegenerations can be traced to such a genetic defect.

In some affections there is already present at birth the loss of function of certain specific cells. Here the inherited absence of certain genes must be assumed. In these cases the loss of the specific function remains unaltered throughout life. Such functional deficiencies are spoken of as heredoconstitutional defects.

In the clinical expression of heredodegenerations and heredoconstitutional defects the visible manifestations are often not of one functional defect but of several, either located in the same organ or separated widely in the body. Some combinations indicate that (1) cells of the same kind which are widely spread are similarly affected, or (2) several defects with different genes are linked together.

In the retina the following cells and tissues are subject to heredodegenerations:

1. The elastic layer of the lamina vitrea, or Bruch's membrane
2. The layer of rods and cones (the neuroepithelium)
3. The inner nuclear layer
4. The ganglion cells

II

The elastic layer of Bruch's membrane forms the termination of the intertwined elastic and collagenous fibrils of the choroid. Although this layer is not a part of the retina, degeneration of this membrane leads to changes in the retina which present distinctly circumscribed clinical entities.

The basal layer of Bruch's membrane is a product of the pigment epithelium. Once formed, the basal layer has a separate existence, and is subject to regular or irregular thickenings which have a distinct ophthalmoscopic appearance and are known as hyaline, or colloid, bodies of Bruch's membrane, and also by the German name of drusen. The function of the basal layer of Bruch's membrane is not clear, and there is nothing known of any change in its function. Ordinarily, the hyaline bodies, even when large, do not interfere with vision, though situated in the macula. When enlarged to a degree where they can displace the rods and cones, some metamorphopsia and a slight reduction in vision may result. The hyaline bodies are therefore not degenerative in the sense in which the term has been defined. However, they do occur to a variable degree even in young people, and are found with greater frequency in advancing age. They are therefore of a hereditary character. Their importance in heredodegenerative diseases consists in the frequency with which they are seen in association with such diseases and thus add to the ophthalmoscopic picture. They are evidently linked with such diseases, although not actually a part of them.

III

The pigment epithelium of the retina is not subject to degenerations on a hereditary basis. In the literature one finds repeatedly the term tapetoretinal degeneration. Presumably, what is meant by this term is the presence of a degeneration of the retina and the tapetum. By the latter term the layer of pigment epithelium is indicated. The term tapetoretinal degeneration is a misnomer, as the tapetum does not undergo a primary degeneration in combination with retinal degeneration. The layer of pigment epithelium does undergo changes in certain forms of heredodegeneration, but these changes are secondary and reactive to the primary changes in the outer layers of the retina.

To follow the changes in the cells of the pigment epithelium layer, it is necessary to have in mind the character of these cells. They are primitive in character, and, aside from their function in presenting a pigment layer for the absorption of light, they possess potentialties similar to those of histiocytes and can serve as phagocytes for the removal of foreign substances in the retina and of the debris and remains of destroyed retinal elements. When there is death of cells in the retina, especially in the outer layers, the cells in the pigment epithelium layer become active. Some of the cells leave the layer,

become ameboid, take on a rounded appearance, shed their pigment, and wander toward the dead elements in the retina, which they engulf and carry toward the blood vessels. There is a proliferation of the pigment epithelium cells, with a diminishing content of pigment. The shed pigment has now become a foreign substance and is removed by the proliferated cells and carried to the perivascular spaces. When the pigment cannot reach the blood stream, it remains in the walls of the vessels.

Such is the reactive action of the pigment epithelium of the retina toward dead cells in the retina, whether the dead cells are the result of a primary degeneration or of any other illness or injury. When such reactive changes occur in the pigment epithelium, there are seen in the fundus of the eye in close proximity depigmented areas, masses of pigment, and, at times, masses of proliferated pigment cells. They indicate reactive activity on the part of the pigment epithelium cells, but not heredodegeneration of this layer as part of a heredodegeneration of the retina.

As a further consequence of the death of cells in the retina, there is apt to be in some forms of heredodegeneration, but not in others, a reactive growth of glia cells and also of connective tissue, the latter derived from the adventitia of the blood vessels. When, as a consequence of the loss of cells in degenerative diseases of the retina, there is a disturbance in nutrition in the neighboring areas, hyalin and lipids are deposited in such areas and form part of the clinical picture.

To summarize, in cases of heredodegeneration of the retina, with the death of cells in the retina, there occur, and can be seen ophthalmoscopically, (1) areas of depigmentation of varying size, (2) accumulation of pigment of varying extent, (3) proliferated pigment epithelium cells, (4) proliferated glia and connective tissue cells of varying extent, and (5) hyalin and lipid deposits.

All the elements mentioned are not necessarily seen in every variety of heredodegeneration, but some are apt to be present in every form. The accompanying hyaline bodies (drusen) of Bruch's membrane are apt to be seen in most varieties of retinal heredodegeneration.

The loss of retinal function, that is, the loss of vision, always corresponds to the extent of the retina affected.

HEREDODEGENERATIONS INVOLVING ELASTIC LAYER OF BRUCH'S MEMBRANE

Degeneration of the elastic layer of Bruch's membrane is characterized by (1) an irregular thickening of the membrane by a tissue accentuation which is fibrillated and, when stained with eosin, resembles collagenous tissue; (2) an inability on the part of the membrane to take the elastic stain in some areas, which then stain poorly or not at all, and (3) breaks in the membrane, which vary in size and number.

These abnormal characteristics of the elastic layer of Bruch's membrane by themselves do not present a clinical picture. However, the secondary changes which follow the breaks in the membrane result in three distinct clinical and pathologic pictures:

1. Kuhnt-Junius disciform macular degeneration
2. Angioid streaks
3. The cases reported by Sorsby and Mason

KUHNT-JUNIUS DISCIFORM MACULAR DEGENERATION

In the central area of the retina, that is, in the region of the macula lutea, plasma or blood transudes from the choriocapillaris through the breaks in Bruch's membrane and lifts up the layer of pigment epithelium. The transudate then passes between the pigment layer and the layer of rods and cones. Now reactive processes follow. There is proliferation of pigment epithelium and of glia, which form a mound in the region of the macula. Fibroblasts and capillaries pass from the choroid through the breaks and by their growth add to the mound. The neuroepithelium in the affected area is destroyed, with corresponding loss of vision. In the vicinity there are apt to be deposits of hyalin and lipid, which are seen ophthalmoscopically as white or yellowish-white, sharply defined exudates in the deeper layers near the

mound. They are not seen in every case. Small hemorrhages on the mound or near by are occasionally seen. Now there is formed the complete picture of Kuhnt-Junius disciform macular degeneration, due to the occurrence of reactive processes following the degeneration and the breaks in the elastic layer of Bruch's membrane. It is remarkable that the formation of a mound following breaks in Bruch's membrane occurs only in the central area of the retina and not in the peripheral parts.

The choriocapillaries in such cases is intact also in the region of the mound. Hyaline bodies (drusen) are usually seen, often in large numbers.

Central vision is correspondingly reduced.

Angioid Streaks

In this disease, which often includes the Grönblad-Strandberg syndrome, there are present the three characteristics of degeneration of the elastic layer of Bruch's membrane. Here, also, there are breaks in Bruch's membrane, and in many cases there is seen the typical mound of tissue in the central area, produced exactly in the same manner as in the cases of Kuhnt-Junius disciform macular degeneration. However, in the cases of angioid streaks and of the Grönblad-Strandberg syndrome there is added a fourth characteristic of degeneration of the elastic layer of Bruch's membrane, namely, basophilia, and the deposit in the membrane of calcium, which can be recognized by the Kossa reaction. Often the presence of iron there can be recognized by the Turnbull blue reaction.

Elastic tissue is particularly prone to calcification, especially following degenerative changes. This is seen in the early deposit of calcium in the intima of arteries of the elastic type, in the isolated calcification of the internal elastic layer of arteries, and in Mönckeberg's media calcification, in which the elastic fibers and the connective tissue are primarily affected. In the cases of angioid streaks there is always basophilia and calcification of the elastic layer of Bruch's membrane. It is this characteristic which is responsible for the ruptures of Bruch's membrane that appear ophthalmoscopically as streaks. According to Verhoeff (1949), the basophilic condition (calcification) brightens the contiguous fundus and makes conspicuous the dark-red choriocapillaris exposed beneath the pigment epithelium by the ruptures. In these cases the choriocapillaris is intact.

Cases of Sorsby and Mason

Another variation in the ophthalmoscopic picture following the degeneration of the elastic layer of Bruch's membrane is presented by the familial cases reported by Sorsby and Mason (1949) under the heading, "A Fundus Dystrophy with Unusual Changes." The affection began in the 40's, with hemorrhages, exudates, and edema in the retina, and progressed to scar formation with a varying amount of pigment deposits. Gradually the process spread peripherally, but left a narrow peripheral zone of retina which was functioning. The presence of a mound is not mentioned. The authors assumed the condition to be genetically a simple autosomal dominant.

With the death of two of the affected patients, Ashton and Sorsby (1951) were enabled to study the eyes histologically. They found that Bruch's membrane was uniformly thickened, that it stained normally with hematoxylin and eosin, and that it showed no basophilia. A section of Bruch's membrane stained with orcein for elastic tissue showed granular degeneration and patchy disappearance of the elastic layer in the posterior polar region. Anteriorly the elastic layer of the membrane stained normally. Kossa's stain for calcium and the Turnbull blue reaction for iron were negative.

In the polar region there were clear-cut breaks in Bruch's membrane. Through these breaks newly formed blood vessels and serous fluid extended from the choroid into the subretinal region. There they formed a partially organized, hyalinized vascular mass, which blended with the degenerated retina.

In addition, there was a marked loss of the choriocapillaris, which was absent posteriorly and atrophic anteriorly. There were also many hyaline bodies (drusen).

These three distinct clinical pictures, (1) Kuhnt-Junius disciform macular degeneration, (2) angioid streaks, and (3) the familial cases of Sorsby and Mason, present variations in the secondary reaction consequent on the heredodegeneration of the elastic layer of Bruch's membrane. In the cases of Sorsby and Mason the loss of the choriocapillaris possibly increased the extent of the retinal lesion. It should be kept in mind that many slight variations of the typical pictures of these diseases possibly occur.

HEREDODEGENERATIONS OF LAYER OF RODS AND CONES (NEUROEPITHELIUM)

The neuroepithelium, specifically the layer of rods and cones, presents typical examples of heredodegenerative and heredoconstitutional diseases. Here, the central area, that is, the area of the macula lutea with its central depression, the fovea, must in any discussion be separated from the extramacular, or peripheral, area. The foveal area acts almost like a distinct organ, especially modified for the highest acuity of vision. It differs from the rest of the retina (1) by the absence of the cerebral layers, which are pushed aside; (2) by the absence of rods; (3) by a change in the character of the cones, and (4) by the relative increase in the number of cones, 160,000 cones in an area of 1 sq. mm., as compared with 132,000 cones in the extrafoveal part of the fundus (Eisler).

HEREDODEGENERATION OF MACULA LUTEA

1.

The visual cells of the region of the macula lutea are the seat of a heredodegeneration which affects them either alone or linked with other heredodegenerations. Here it is the gradual dissolution and final disappearance of the cones which cause the loss of the functional element, the acuity of vision. And here, again, it is the reactive changes, the depigmentation, pigmentation, and proliferation of pigment cells, grouped together in the small central area, which characterize the ophthalmoscopic picture. Proliferation of glia is only seen in an occasional case. Hyaline bodies of Bruch's membrane (drusen) are a very frequent accompaniment, although not seen in every case.

There are on record only a few cases of heredodegeneration of the macula with a pathologic study. The most recent and best is that by Klien of a woman aged 60 with bilateral macular degeneration. In this case there was seen in the region of the macula an area in which the neuroepithelium was completely missing. In a small area the pigment epithelium was lacking (depigmentation) and small groups of pigment cells were lying here and there. There were also defects of only a few visual cells, and at the site of these defects there were alterations in pigment. The choriocapillaris was intact.

Fundamentally, then, heredodegeneration of the retina in the region of the macula lutea is characterized clinically by a reduction in central vision, and ophthalmoscopically in a typical case by an area in which pigmentation and depigmentation are sharply limited to the region of the macula. A number of local variations occur: (1) All possible variations occur in the arrangement of the pigment deposits and the depigmented areas; (2) the color of the depigmented spots varies from white to gray to yellow; (3) the extent of the lesion may reach for a little distance beyond the limit of the macula lutea, and (4) the accompanying hyaline bodies (drusen) are of a varying extent and may cover the macular lesion, so that only the reduction of vision indicates that a heredodegeneration of the retina is present in the macula.

The heredodegeneration is usually bilateral, but unilateral involvement is occasionally seen. In a case under my observation for years, one eye only is involved. Berkley and Bussey (1949) reported a family with heredodegeneration of the macula which included a boy of 14 years in Generation III and a boy of 8 years in Generation IV. In the left eye of each of these boys there was a heredodegeneration of the macula. Vision with correction was noted as 20/20 in the right eye of each, which is obviously incompatible with degeneration of the retina in the macular region. By inference, at the time of

the report there was no degeneration in the macula of the right eye of either of these boys, so that a unilateral heredodegeneration must be assumed until time proves otherwise.

II

It is unfortunate for the understanding of heredodegeneration of the macula that the variations in the ophthalmoscopic picture have given rise to classifications of separate disease entities, to each of which the name of the first observer is attached. Such separate entities are known as Tay's choroiditis, Doyne's honeycomb choroiditis, Best's congenital macular degeneration, Stargardt's disease, Behr's disease, and various others. It should be realized that in heredodegeneration of the macular region of the retina, the gradual degeneration and disappearance of the cones there is the one essential element, and that the reactive processes of depigmentation, proliferation of the pigment epithelium, and perhaps a change in the glia, together with the presence of hyaline bodies, are responsible for all the variations in the ophthalmoscopic picture. It is clear, then, as it was to Behr, that there is only one heredodegeneration of the macula and that only the time of life when the degeneration begins differentiates the manifestations of the disease. Heredodegeneration of the macula begins in some families in infancy, a rare occurrence. It begins more frequently at the age of 6 to 8 years, or at puberty; in other cases, in the 20's or 30's. There is also a presenile form, beginning in the 40's or 50's, and there is the commoner senile macular degeneration.

Another differentiation is the character of the heredity. Dominant, recessive, and sex-linked forms of inheritance have been observed (Falls, 1949, 1950).

III

Typically, heredodegeneration of the macula occurs by itself. In some cases it occurs in association with other affections of the retina, or of the central nervous system. Such an association does not mean that we are dealing with a new disease or a new variant. It means that heredodegeneration of the macula is linked genetically with heredodegenerations in which other genes are involved. Each affection is independent of the other. Hereditary diseases which are ocasionally seen in association with heredodegeneration of the macula are (1) degeneration of the extramacular regions of the retina, (2) atrophy of the optic nerve, (3) color blindness, and (4) mental deterioration.

Primary Pigmentary Degeneration of Retina

I

Primary pigmentary degeneration presents the classic picture of heredodegeneration of the layer of rods and cones in the periphery. There is a gradual degeneration of and disappearance of the rods and cones, beginning in the equatorial region and spreading peripherally and centrally. As the rods here by far outnumber the cones, the loss of function is expressed by night blindness, peripheral scotomata, and a reduction or absence in dark adaptation, that is, by the preponderant loss of rods.

The ophthalmoscopic picture is characterized by (1) pallor of the optic disc, (2) narrowing of the retinal vessels, (3) pigment deposits in the retina and on the retinal veins, and often (4) visibility of the choroidal vessels. Hyaline bodies (drusen) are frequently seen.

Pathologically, it has been shown that, beginning at the equator and spreading peripherally and centrally, there is at first a gradual loss of the outer members of the rods and cones, then of the inner members, followed by the disappearance of the nuclei in the outer nuclear layer. While the loss of function of the peripheral parts of the retina and the loss of dark adaptation are explained by the loss of the neuroepithelial elements, the ophthalmoscopic picture is only partly explained by the reactive changes following the loss of these elements.

With the degeneration and destruction of the rods and cones and the consequent presence of their debris, the following sequence of events takes place: 1. Cells of the pigment

epithelium layer begin to proliferate and acquire ameboid mobility; cells leave the layer and new cells take their place. *2.* The ameboid cells are converted into phagocytes and engulf the debris of the rods and cones and carry it to the vessels. The cells lose their pigment, which remains in the retina where they have been shed, or where the phagocytes have died while moving. In time, in the course of years, there accumulates an assemblage of pigment in regular or irregular formation. *3.* The shed pigment, which now constitutes a foreign substance, is engulfed by the proliferated nonpigmented cells and carried to the vessels. Here these cells surround the vessels, and that part of the pigment which does not reach the lumen of the vessels to be carried away remains in the perivascular spaces and is visible in the fundus. Some of the vessels become hyalinized.

These processes explain the presence of visible masses of pigment in the retina and on the vessels. The diminished content of pigment in the cells of the pigment epithelium layer explains the visibility of the choroidal vessels. There is also a proliferation of glia and of Müller's fibers, but this is not noticeable with the ophthalmoscope. The optic disc frequently shows a proliferation of glia.

The reactive processes mentioned do not explain the narrowing of the vessels, which is an essential element in primary pigmentary degeneration. No satisfactory explanation has been found for the narrowing of the retinal vessels, and it is not easy to see how this narrowing is in any way related to the degeneration of the rods and cones. It remains one of the unsolved problems of this disease.

That the primary element in primary pigmentary degeneration is the degeneration and disappearance of the neuroepithelial elements, especially of the rods, is also shown by the exact studies of Mandelbaum (1941) on dark adaptation in this disease. These studies show that rod function is diminished to a much greater extent than cone function, and that in an advanced stage no sign of rod function may be found. The loss of function of the visual cells is reflected in the electroretinogram, which responds with the extinguished form (Björk and Karpe, 1951; Jacobson and O'Brien, 1953; Riggs, 1954).

II

The character of inheritance in primary pigmentary degeneration is of importance. The disease is inherited (1) as a Mendelian recessive, the most frequent form of heredity; (*2*) as a dominant, which is much less frequent, and (3) as a sex-linked recessive, a rare form of heredity. Falls (1950) mentioned also incomplete sex-linked recessive and dominant modes of heredity. He also reported with Cotterman (1948) a case of primary retinal degeneration in which it was assumed that the disease was the result of an intermediate sex-linked x-borne trait.

Primary pigmentary degeneration, heredodegeneration of the neuroepithelium in the periphery of the retina, is at times linked with other heredodegenerations. In some of these the linkage is incidental and does not occur in every case. In others the linkage seems to be a firm association and the primary pigmentary degeneration is always a characteristic part of the disease.

The following incidental linkages are encountered:

1. Heredodegeneration of the macula. The typical ophthalmoscopic picture of each of the two diseases can be shown to be separated by a narrow strip of normal retina. Or the two pictures merge into one another. François (1949) reported and illustrated the cases of a brother and a sister, where the brother suffered from heredodegeneration of the macula, and the sister had in addition primary pigmentary degeneration.

2. Deaf-mutism. This combination seems to occur only in the cases with a recessive mode of heredity. Deafness also is apt to be linked in this mode of heredity.

3. Mental deficiency and other diseases of the central nervous system. These are occasionally linked with the recessive form.

4. Color blindness.

The diseases in which primary pigmentary degeneration always constitutes a part of the clinical picture are as follows:

1. The Laurence-Moon-Biedl syndrome. The complete clinical picture consists of primary pigmentary degeneration, obesity, genital dystrophy, polydactyly, mental deterioration, and familial occurrence. In the cases collected by Reilly and Lisser (1932) primary pigmentary degeneration was seen in 61 out of 77.

2. Juvenile amaurotic family idiocy.

3. The late infantile type of amaurotic family idiocy.

Gyrate Atrophy of Choroid and Retina

There are two hereditary disease entities, heredodegenerations, in which the neuroepithelium of the retina suffers together with the choroid: (1) gyrate atrophy of the choroid and the retina, and (2) choroideremia.

Gyrate atrophy frequently affects several members of a family and may begin in childhood with night blindness. Ophthalmoscopically, in a typical case there are seen in the fundus areas of atrophy which enlarge gradually and are separated by strands of normal red fundus. In the atrophic areas the white sclera is seen, together with remnants of choroidal vessels and scattered clusters of pigment. As the atrophy progresses and more and more of the choroid and of the outer layers of the retina is lost, the visual field is correspondingly constricted, and vision decreases to light perception only.

There is no record of a pathologic study of this disease. It is obviously a familial heredodegenerative disease in which there is a slowly progressive atrophy of the choroid and of the outer layers of the retina. The mode of heredity is an autosomal recessive. It is difficult to tell in what relation the disease stands to primary pigmentary degeneration. It is known that the disease is found occasionally in a member of a family in which primary pigmentary degeneration is present in other members. Franceschetti (1954) mentions a case of a woman 57 years of age with primary pigmentary degeneration in the right eye and gyrate atrophy in the left eye. The electroretinogram of the right eye showed no response, a finding which is characteristic of primary pigmentary degeneration, while the response in the left eye was subnormal, but nevertheless quite good.

Choroideremia

Choroideremia is a disease in which there is congenital absence of the choroid and of the outer layers of the retina. The defect involves the greater part of the extramacular area, leaving the macula normal. In an occasional case there remain several areas of normal choroid and retina. Such are the cases of the brothers G III and G IV of the family reported by Sorsby, Franceschetti, Joseph, and Davey (1952). The retained normal part of the fundus, whether macular or extramacular, gradually undergoes degeneration, with the final disappearance of the normal area. The disease is thus a congenital and progressive affection on a hereditary basis.

The hereditary character of the disease was discovered by McCulloch and McCulloch (1948) and confirmed by Sorsby and his associates (1952). It is an intermediate sex-linked x-borne gene trait, in which the heterozygous, or carrier, female exhibits a slight amount of pigmentary change in the fundus and does not suffer from any ocular symptoms. The affected males exhibit the full clinical picture of the disease, as follows:

There is a history of night blindness since childhood. The visual fields are contracted. Vision varies from normal to finger counting only. Ophthalmoscopically, in a typical case, the fundus is glistening white with a more or less normal macula. The choroidal vessels are absent, and there are scattered flecks of pigment. The retinal vessels are normal, and the optic disc is of a normal color, or slightly pale. In some cases a considerable number of choroidal vessels are to be seen. In time the normal parts of the fundus also disappear, with a corresponding reduction in vision.

There is only one pathologic report of this disease, by J. C. McCulloch (1950). At the ora serrata the pigment epithelium was intact; there was cystoid degeneration of the retina, and the choroid was present. Posteriorly, the pigment epithelium had become a pigmented line, and the choroid was seen as a fibrous strand containing sclerosed vessels. Bruch's membrane was present. Halfway to the posterior pole from the ora serrata, the choroid and Bruch's membrane had disappeared completely. The layers which could be identified were those of the sclera, the bipolar cells, the inner plexiform layer, the ganglion cells, the nerve fibers, and the internal limiting membrane.

In the region of the macula some choroid was again present. It appeared as a thin strand, containing an occasional patent vessel with thickened walls. A small area showed pigment epithelium, cone fibrils, the outer nuclear layer, the remnant of Henle's fiber layer, bipolar cells, and the inner layers of the retina. The ganglion cells were intact and about six cells deep. The inner layers showed a cystic degeneration, which extended into the optic disc and into the neighboring parts of the optic nerve.

The histologic sections, as illustrated by McCulloch, showing the bipolar cells lying against the sclera, give the impression that the missing layers have always been absent. I conceive the disease, as does Nettleship, to be a congenital deficiency of the choroid and the outer layers of the retina, with that part of the choroid and outer layers of the retina which are still present subject to a gradual, slow degeneration.

HEREDOCONSTITUTIONAL DEFECTS OF NEUROEPITHELIUM

So far I have discussed heredodegenerative diseases of the neuroepithelium of the retina. There are also heredoconstitutional defects which affect the scotopic system, that is, the rods in the extramacular retina. These are (1) congenital night blindness without fundus changes; (2) Oguchi's disease, and (3) retinitis punctata albescens. In all these three diseases the chief symptom is night blindness, which is present from birth. The diseases remain stationary throughout life, and there are no secondary reactions due to any activity on the part of the pigment epithelium or to any glia proliferation, such as is seen in heredodegenerative diseases. In all these diseases there is a congenital and inherited defect in the rods which prevents them from exercising their function. It must be assumed that the primary defect is in the gene or genes, which may possibly consist in their total absence. These diseases are of rare occurrence in the United States.

CONGENITAL NIGHT BLINDNESS WITHOUT FUNDUS CHANGES

Visual acuity, visual fields, and color vision are usually normal in full daylight. With reduced illumination vision is reduced or completely abolished. With slight reduction in illumination, when vision is still present, there may be a marked contraction of the visual fields. Dark adaptation is practically nonexistent. Ophthalmoscopic examination is completely negative. The optic disc is of a normal color; the retinal vessels are of a normal caliber, and there is no pigmentation anywhere in the fundus as part of the clinical picture. The electroretinogram shows an absence of the b-wave, which is indicative of the absence of rod function. In the Cases L and F of Dr. F. D. Carroll, in which an electroretinographic study was made by Riggs (1954), there was found absence of the b-wave, but the a-wave was present. As the a-wave is considered to be due to the function of the cones, the electroretinogram in these cases is added evidence that only the rods are functionally defective.

The mode of inheritance of this disease is in three forms: (1) as a dominant, (2) as a recessive, and (3) as a sex-linked recessive. The dominant form, or Nougaret form (from the ancestor of the most important family of this type), is not associated with other heredoconstitutional defects and is not associated especially with myopia. The recessive form is often associated with myopia.

Oguchi's Disease—Congenital Night Blindness with Grayish-White Discoloration of Fundus

Oguchi's disease is a congenital form of night blindness in which there is seen in the fundus a grayish-white discoloration, which disappears when the patient remains in the dark for several hours (Mizuo's phenomenon). In the daylight the discoloration gradually reappears. To a certain degree some rod function is still present.

There are cases of transition from congenital blindness without fundus changes to the cases with the grayish-white discoloration. Oguchi's first case was one in a sibship of eight, in which two other sibs had Oguchi's disease and two others had night blindness. Cataract, myopia, and mental defectiveness were also found in this sibship. The parents were first cousins. The disease is inherited as an autosomal recessive and remains stationary throughout life.

There is only one pathologic report of this disease, that of the case in which Mizuo's phenomenon was first observed. Oguchi's findings follow: (1) A change in the distribution of the cones. The area in the retina in which cones alone practically were found extended from the foveal area to about 20 degrees temporally. Oguchi classed the change as an atavistic one phylogenetically. There were also found a larger-than-normal number of cone nuclei lying outside the external limiting membrane. (2) A close connection between the outer end of the visual cells and the pigment epithelium cells. This was responsible for the separation of an artificial layer histologically between the layer of rods and cones and the layer of pigment epithelium cells. There was evidently no histologic abnormality to be seen in the visual cells outside the extended cone area, and there were no reactive processes on the part of the pigment epithelium cells or of the glia cells.

There is as yet no adequate explanation for the existence of the grayish-white discoloration in the fundus and for its disappearance after remaining several hours in the dark.

Retinitis Punctata Albescens

This is the third heredoconstitutional disease with congenital night blindness. Here, also, the disease remains stationary throughout life. Central vision may be normal or only slightly reduced. The visual fields are normal in daylight or bright illumination but are contracted in reduced illumination. In a study of dark adaptation, Mandelbaum (1941) found in one case 7.00 log units for the cone threshold (which is normal), no rod threshold, and a photochromatic interval of zero. There was evidently no rod function at all.

Ophthalmoscopically, the disc is of a normal color and the retinal vessels are of a normal caliber, or only slightly narrowed. There are no reactive phenomena on the part of the pigment epithelium or of the glia. The fundus differs from one of congenital night blindness without fundus changes by the presence there of innumerable discrete white dots, round, sharply demarcated, free from pigment, "dull or dead-white like paint" (Nettleship).

There is no pathologic report of this disease, and the histology of the white dots is definitely not known. The heredity is that of an autosomal recessive. In this, as in the other two heredoconstitutional diseases, the primary defect must be in the gene or genes which control the processes underlying rod function. There is some relationship between this disease and primary pigmentary degeneration. Cases of retinitis punctata albescens have been found to occur in families in which other members were affected with primary pigmentary degeneration.

Heredodegenerations of Inner Nuclear Layer

Cystoid Degeneration of Retina

I have discussed so far the heredodegenerations which involve Bruch's membrane and the neuroepithelium. Heredodegeneration also involves the inner nuclear layer, and secondarily the internuclear layer. The degeneration shows itself by the gradual disappearance of the cells of the inner nuclear

layer, their places being taken by a fluid. Such cystoid spaces also appear in the internuclear layer and occasionally in the inner part of the outer nuclear layer. Leber called it cystoid degeneration. The cystoid spaces enlarge by coalescence, with the disappearance of the septa.

Cystoid degeneration occurs secondary to other diseases of the retina. However, it also occurs as a primary heredodegeneration, as part of the aging processes. As such, it is found in the anterior end of the retina near the ora serrata. While it has been seen in children, it is found more and more frequently in advancing age. In addition to its predilection for the periphery of the retina, cystoid degeneration is apt to occur in the region of the fovea, where the retina is avascular. Wherever situated, the retina is thickened by the cystoid spaces. The anterior and posterior walls of the spaces become extremely thin and rupture easily, with the formation of tears. Especially in the region of the fovea, the anterior walls of the cystoid spaces are gradually absorbed, forming an incomplete hole, or the whole thickness of the cystoid spaces is absorbed, with the formation of a typical hole in the center of the macula. In histologic sections the hole shows rounded edges.

Such a sharply defined hole in the macula, which on ophthalmoscopic examination can be easily recognized as a hole, is seen in elderly people, and rarely in young persons. It is more often unilateral, but it is occasionally also seen bilaterally, as the end-result in a cystoid degeneration. Such a cystoid degeneration, which is not the result of a trauma or of a circulatory or an inflammatory process, must necessarily be the final stage of an inherent hereditary defect. Such a hole in the macula seldom gives rise to a detachment of the retina.

The holes and tears in the retina which lead to a detachment of the retina are also the end-result of a cystoid degeneration. In these cases the cystoid degeneration is widespread and may involve the whole retina. Often it can be seen in histologic sections that the hole has rounded edges, indicating the gradual development of the hole. Many ophthalmologists assume additional causative factors in the formation of a hole or a tear in the retina, such as strands in the vitreous exercising a pull on the retina. However, holes in the retina leading to detachment can be formed without such traction. The fundamental element here is the degeneration of the inner nuclear layer, with involvement also of the internuclear layer, leading to the formation of cystoid spaces. Such a degeneration, aside from the aggravating effect of a progressive myopia, must necessarily be hereditary (Vontobel, 1929).

Retinitis Circinata

Cystoid degeneration of the retina constitutes the basis of retinitis circinata. This disease is characterized (1) by a thickening of the macular region which is more or less opaque and of a gray or yellowish color, and (2) by a girdle of white exudates in the deeper layers of the retina situated at a short distance from the macula. Central vision is correspondingly reduced.

I know of only five cases in which the pathologic changes have been reported. In all of them there was found a cystoid degeneration of the retina involving the area occupied by the girdle of exudates and the area enclosed within the girdle. The cystoid spaces cause a thickening of the macular region. They are filled with a hyaline substance and lipids. Where the white exudates are seen ophthalmoscopically, the retina contains a large number of fat granule cells, which seem to engulf the hyaline exudates and the lipids. The fat granule cells are derived in part from the proliferated pigment epithelium cells and in part from glia cells.

The essential element in retinitis circinata is the cystoid degeneration of the inner nuclear layer and the secondary affection of the internuclear layer. The disease must be considered as a degeneration on a hereditary basis, although there are no heredity studies of this disease.

HEREDODEGENERATION INVOLVING GANGLION CELLS OF RETINA

Degeneration of the ganglion cells of the retina occurs as the end-result of a metabolic disturbance in these cells with the accumulation in them of prelipid substances, which the cells are unable to utilize. This metabolic disturbance affects ganglion cells in the whole of the nervous system, both central and peripheral, and the ganglion cells of the retina are affected with them. More specifically, it is the neuron which is affected. The cell body of the neuron is enlarged and rounded. The Nissl bodies have disappeared for the greater part, and the remnant is pressed against the eccentric nucleus. The neurofibrils are pushed to one side, and the rest of the cell is filled with prelipids. Several of the dendrites in their portion near the cell body are similarly affected. The prelipoid granules stain a faint pink or yellow-red with scarlet red and Sudan stains. The increased content of the cell finally compresses the neurofibrils, and the neuron eventually degenerates.

With the gradual destruction of the neuron the glial and mesenchymal elements become activated. With fat stains, neutral fat is found in the microglial cells. The fat has been liberated from the degenerated neurons and taken up by the glia cells, and probably also by mesenchymal cells. These cells carry their load to the perivascular spaces, which become filled with fat-laden cells.

The central element is the inability on the part of the ganglion cells to utilize the prelipids, which therefore, accumulate in the cells and after a time prevent the cells from exercising their normal function. The changes in the glia and mesenchymal cells are secondary.

The diseases in which there are found the characteristic changes in the ganglion cells are as follows:

1. Infantile amaurotic family idiocy, or Tay-Sachs disease
2. Juvenile amaurotic family idiocy (Vogt-Spielmeyer or Stock-Spielmeyer type)
3. The late infantile amaurotic family idiocy (Bielschowsky, or Batten-Mayou type)
4. Niemann-Pick disease

Infantile Amaurotic Family Idiocy, or Tay-Sachs Disease

In this type the characteristic changes in the ganglion cells are found throughout the whole central and peripheral nervous systems. These changes occur also in the ganglion cells of the retina, which contain the prelipids. They have been found by Hagedoorn (1940) and by MacMillan (1948) in the cells of the inner nuclear layer. The other layers of the retina, including the layer of rods and cones, are not affected in Tay-Sachs disease.

Ophthalmoscopically, there is seen in the fundus of the eye a white to grayish-white area in the macular region, in the center of which the fovea is seen as a cherry-red spot. There is amaurosis.

The clinical picture is characteristic. The child develops normally until about the third to the sixth month, when it becomes dull and apathetic. There are disturbances in movements, and the child cannot hold up its head. In a short time the child is blind. In some cases there are convulsions. There are hyperesthesia and hyperacusis, and there develop gradually the signs of decerebrate rigidity. Death occurs within the second or third year.

The disease is familial, and therefore hereditary. According to Franceschetti (1930), the relation of diseased children to nondiseased children in families, as gathered from the literature, is apt to speak for a dominant mode of heredity. However, with the occurrence in some cases of parental consanguinity, he assumes also a recessive mode of heredity, in addition to a dominant. The disease has been found more frequently among Jews from Eastern Europe.

The nature of the prelipoid substance which accumulates in the ganglion cells in infantile amaurotic family idiocy seems to have been elucidated by Klenk (1941, 1947). He found in his fractionations of the brain lipids a phosphorus-free lipid containing carbohydrate which he named ganglioside. From it

Klenk isolated a hydrolysis product which he named neuraminic acid. In Tay-Sachs disease the ganglioside content of the total solids of the brain was found to be 4% to 8%, in contrast to 0.3% in normal brains. It must be assumed that there is an abnormality in the gene or genes which has to do with enzymatic activities of the ganglioside in the cells of the nervous system.

The grayish-white area in the macular region of the retina can be explained only on the basis of an increased lipoid content of the ganglion cells, which are densely accumulated there.

Juvenile Amaurotic Family Idiocy (Vogt-spielmeyer or Stock-Spielmeyer Type)

Juvenile amaurotic family idiocy is familial and is of a characteristic uniformity. The child develops normally until about the fifth to the eighth year, when there is a gradually progressive loss of vision. In one to two years vision is diminished to finger counting or to light perception only. With the onset of the visual disturbances there occur epileptiform convulsions, other neurologic symptoms, and a gradually progressive dementia of the imbecile type. The end-stage is blindness, complete idiocy, and helplessness. Death usually occurs about the age of 18 years.

In this type, also, the characteristic changes in the ganglion cells are found throughout the nervous system. However, the cells are unevenly affected, so that side by side with many diseased ganglion cells there are many that are quite normal. In the retina the ganglion cells are affected in the same manner as the ganglion cells in the rest of the nervous system. Specific for this type is the additional involvement of the neuroepithelium. There is the gradual disappearance of the rods and cones associated with the loss of the nuclei of the outer nuclear layer. There is proliferation of the pigment epithelium and of glia elements.

Ophthalmoscopically, there is found the typical picture of primary pigmentary degeneration.

The character of the heredity is the subject of an intensive study by Sjögren (1931). He concluded that the disease follows a recessive monohybrid mode of heredity and that the heredity-biologic characteristics differ entirely from those of Tay-Sachs disease. Since in the juvenile type the affection of the ganglion cells is linked with an affection of the visual cells, it should be assumed that there is a linkage of the genes which have to do with the activities of these various cells. Klenk found the ganglioside content of the total solids of the brain to be 1.5% in this disease, as contrasted with 0.3% in the normal brain and 4% to 8% in the brains of Tay-Sachs disease.

Late Infantile Amaurotic Family Idiocy (Bielschowsky, or Batten-Mayou Type)

The late infantile type of amaurotic family idiocy corresponds in character to the juvenile type. It differs from the juvenile form in that the disease begins in the fourth year of life and usually ends in death in about four years. The cases reported by Batten and Mayou were studied histologically and showed the characteristic changes in the ganglion cells, together with the loss of rods and cones and with secondary pigmentary changes. The disease is thus a variation of the juvenile type and does not represent a transition form between the infantile and the juvenile type.

Niemann-Pick Disease

This disease resembles infantile amaurotic family idiocy (Tay-Sachs disease) in part of its clinical picture and in the affection of the ganglion cells in the central and peripheral nervous systems. The child may develop normally for the first six months of life, but the disease has also been found at birth. There is first noted an enlarged abdomen, due to the enlargement of the liver and the spleen. The skin is grayish-brown; there is loss of subcutaneous fat, and the lymph nodes are enlarged and hard. The child begins to lose weight, becomes emaciated, is unable to sit up or hold up its head, and moves very little; gradually all movements cease. There

is amaurosis. Death is due to exhaustion or to an intercurrent infection in the second or third year. Characteristic of this disease is the presence in various organs of the "foam" cell, or Pick cell, derived from the endothelial and reticular cells and containing lipids. The cells appear also in the blood stream.

In a number of cases of Niemann-Pick disease there is seen in the fundus of the eye the typical picture of the Tay-Sachs cases: a white or grayish-white area in the macular region in the center of which the fovea appears as a cherry-red spot.

The ganglion cells of the nervous system have the typical appearance of the ganglion cells in amaurotic family idiocy and are filled with prelipids. In Niemann-Pick disease the prelipoid is sphingomyelin.

In the retina the ganglion cells show the typical changes, due to their large content of sphingomyelin. Didion observed the disease in twins of non-Jewish parentage from the age of one year until death. One died at the age of 16½ months, and the other at 31½ months. At the age of 14 months both twins showed the typical picture in the fundi of the eyes, the cherry-red spot surrounded by the grayish-white area. Histologically, there were seen in the retina the changes in the ganglion cells and similar changes in the bipolar cells in the inner zone of the inner nuclear layer. In this disease, as in Tay-Sachs disease, the grayish-white area in the macular region of the retina is due to the content of prelipids (in this case, of sphingomyelin) in the ganglion cells of this region.

Niemann-Pick disease must be considered as the result of an inherent defect in the gene or genes controlling the enzymatic processes in the metabolism of sphingomyelin in the ganglion cell of the nervous system, and probably in the cells of other organs as well.

SUMMARY AND CONCLUSIONS

An attempt is made to circumscribe more sharply the individual heredodegenerations of the retina.

By heredodegeneration is understood the gradual disappearance without any external cause of certain cells or parts of tissues, and the premature death of such cells or parts of tissues, for which Gowers introduced the term abiotrophy.

In the retina the following elements are the seat of heredodegenerations: (*a*) the elastic layer of Bruch's membrane; (*b*) the neuroepithelium, that is, the layer of rods and cones; (*c*) the cells of the inner nuclear layer, and (*d*) the ganglion cells.

The visual disturbance in each heredodegeneration is due to the loss of the visual cells. The ophthalmoscopic picture is the result of the reactive process on the part of the pigment epithelium cells, of depigmentation of these cells, and of proliferation of glia.

Heredoconstitutional defects which affect the visual cells produce visual disturbances without any proliferative processes of the cells of the pigment epithelium or of the glia.

The cells of the pigment epithelium are not the seat of any heredodegeneration.

BIBLIOGRAPHY

Ashton, N., and Sorsby, A.: Fundus Dystrophy with Unusual Features, Brit. J. Ophth. **35**:751, 1951.

Berkley, W. L., and Bussey, F. R.: Heredodegeneration of the Macula, Am. J. Ophth. **32**:361, 1949.

Björk, A., and Karpe, G.: The Clinical Electroretinogram: The Electroretinogram in Retinitis Pigmentosa, Acta ophth. **29**:361, 1951.

Bounds, G. W.: The Electroretinogram: A Review of the Literature, A. M. A. Arch. Ophth. **49**: 63, 1953.

Didion, H.: Die anatomischen Veränderungen des Augenhintergrundes bei der Niemann-Pickschen Krankheit, Klin. Monatsbl. Augenh. **116**:131, 1950.

Falls, H. F.: Hereditary Macular Degeneration, Am. J. Human Genet. **1**:96, 1949.

Genetics, in Symposium: Primary Chorioretinal Aberrations with Night Blindness, Tr. Am. Acad. Ophth. **54**:617, 1950.

——and Cotterman, C. W.: Choroidoretinal Degeneration: A Sex-Linked Form in Which Heterozygous Women Exhibit a Tapetal-Like Retinal Reflex, Arch. Ophth. **40**:685, 1948.

Franceschetti, A.: Die Vererbung von Augenleiden, in Schieck, F., and Brückner, A.: Kurzes Handbuch der Ophthalmologie, Berlin, Springer-Verlag, 1930, Vol. 5, p. 772.

Franceschetti, A., in General Discussion on the Electroretinogram, Am. J. Ophth. **38**:90 (July, Pt. II) 1954.

François, J.: Contribution à l'étude des hérédo-dégénérescences tapéto-rétiniennes (dégénérescence choriorétinienne familiale à hérédité dominante: Coexistence familiale de la dégénérescence pigmentaire de la rétine et de la maladie de Stargardt), Ophthalmologica **118**:1, 1949.

Hagedoorn, A.: Amaurotic Family Idiocy and Related Conditions, Am. J. Ophth. **23**:735, 1940.

Jacobson, J. H., and O'Brien, J. M.: Electroretinographic Studies in Cases of Pigmentary Degeneration, A. M. A. Arch. Ophth. **49**:375, 1953.

Klenk, E.: Neuraminsäure, das Spaltprodukt eines neuen Gehirnlipoids, Ztschr. physiol. Chem. **268**:50, 1941.

Über die Verteilung der Neuraminsäure im Gehirn bei der familiären amaurotischen Idiotie und bei der Niemann-Pickschen Krankheit, Ztschr. physiol. Chem. **282**:84, 1947.

Klien, B. A.: Heredodegeneration of the Macula Lutea, Am. J. Ophth. **33**:371, 1950.

McCulloch, J. C.: Pathologic Changes in Two Cases of Choroideremia, Tr. Am. Acad. Ophth. **54**:565, 1950.

——and McCulloch, R. J. P.: A Hereditary and Clinical Study of Choroideremia, Tr. Am. Acad. Ophth. **52**:160, 1948.

MacMillan, J. A.: Histology of Retina in a Case of Tay-Sachs Disease, Am. J. Ophth. **31**:1567, 1948.

Mandelbaum, J.: Dark Adaptation: Some Physiologic and Clinical Considerations, Arch. Ophth. **26**:203, 1941.

Reilly, W. A., and Lisser, H.: Laurence-Moon-Biedl Syndrome, Endocrinology **16**:337, 1932.

Riggs, L. A.: Electroretinography in Cases of Night Blindness, Am. J. Ophth. **38**:70 (July, Pt. II) 1954.

Sjögren, T.: Die juvenile amaurotische Idiotie; klinische und Erblichkeits-medizinische Untersuchungen, Hereditas (Lund), **14**:197, 1931.

Sorsby, A.; Franceschetti, A.; Joseph, R., and Davey, J. B.: Choroideremia, Clinical and Genetic Aspects, Brit. J. Ophth. **36**:547, 1952.

——and Mason, M. E. J.: A Fundus Dystrophy with Unusual Features, Brit. J. Ophth. **33**:67, 1949.

Verhoeff, F. H.: Histological Findings in a Case of Angioid Streaks, Brit. J. Ophth. **32**:531, 1949.

Vontobel, E.: Untersuchungen über die Vererbung der myopischen Fundusdegeneration, von Graefes Arch. Ophth. **122**:311, 1929.

Gas Gangrene Panophthalmitis

Review of the Literature; Report of New Cases

ROBERT B. LEAVELLE, M.D., North Hollywood, Calif.

Panophthalmitis due to organisms of the gas gangrene group is fortunately a rare affliction. Twenty-four authors have described a total of 53 cases since 1904. Seven of these occurred in the United States, the first being recorded in 1932. This report adds three more cases.

Certain characteristics common to every reported instance of gas gangrene panophthalmitis were noted:

1. Infection followed a perforating wound of the globe.

2. Despite any and all therapeutic measures undertaken, the infection progressed, destroying all visual function.

3. The infected globe was either eviscerated or enucleated, or the entire orbit exenterated.

4. Postoperative recovery was essentially uneventful and complete.

SUMMARY OF REPORTED CASES

Clinical Course

The majority of these cases gave the history of a perforating injury which occurred while hammering or chipping metal or stone. In a large percentage the patient did not realize the eye had been penetrated by a foreign body, considering the incident trivial. The subsequent course of the injury and consequent panophthalmitis in each case was remarkably similar, regardless of the magnitude of the original injury. The three cases of Lutz[10] were the exception, in that the usual fulminating course apparent in the others was not evident.

Symptoms and Signs.—Pain and rapid loss of vision occurred within twelve hours following the injury. A violent panophthalmitis with chemosis and brawny swelling of the lids was usually apparent by 18 hours. Amaurosis, proptosis, hypopyon, ring abscess of the cornea, coffee-colored discharge, gas bubbles in the anterior chamber, rise in the intraocular tension, immobilization of the globe, necrosis of the wound margins, and a total loss of fundus reflex were signs usually evident by 24 hours. Systemic reactions of fever, prostration, leucocytosis, glycosuria, nausea, and vomiting usually occurred after the first 24 hours, and were generally not as proportionately severe as the local reaction.

Diagnosis.—The diagnosis was suspected clinically within 24 hours in several cases,* but was not established by laboratory means in any case until after 48 hours following the injury. When a foreign body was found, by x-ray or surgically, it was invariably in the vitreous.

Treatment.—The treatment employed was, in general, empirical. Heath[12] was the first to use gas gangrene antitoxin as an attempted therapeutic procedure, and antitoxin was subsequently administered to 19 other patients.† Typhoid vaccine[17] and milk injections‡ were also employed as therapeutic measures. Apparently, Capus[24] was the first

From the Massachusetts Eye and Ear Infirmary, Boston.

Drs. Albert H. Sloane, Henry F. Allen, and Bernard H. Zeavin permitted the report of cases under their care.

* References 12, 13, 14, and 21.

† References 13, 14, 16, 17, 21, 22, 24, 25, and 28. Thygeson, P.: Ocular Bacteriology: A Manual of Lecture Notes; Account of Case, Briefly Reviewed circa 1950, unpublished.

‡ References 19 and 20.

to use sulfonamides and penicillin systemically in a case of gas gangrene panophthalmitis, and in this case administration of both was started early. The six cases reported subsequent to this § also received antibiotics and/or chemotherapy. Chlortetracycline (Aureomycin) was administered topically to two patients.‖ Removal, or attempted removal, of a foreign body from the vitreous was reported in about one-third of the series.

End-Result.—This was the same in all cases: the complete disorganization of the visual function by the pathologic process, and the final necessity for evacuation of the destroyed tissues by surgical means. In two cases ¶ it was necessary to exenterate the orbit to control the infection. In one of these [23] the globe had been enucleated first. Of the remaining 51 cases, about two-thirds had evisceration, one-third enucleation. In no case was there a spread of the infectious process beyond the orbital tissues. Recovery was essentially uneventful and complete after surgical evacuation, and did not appear to differ significantly, regardless of the technique employed, the time surgery was done, or various therapeutic measures used before or after surgery. Kennedy and Vogel [28] felt that the usual violent course of this type of panophthalmitis had been attenuated by intensive systemic penicillin therapy.

§ References 25, 26, 27, 28, 29. Thygeson, P.: Ocular Bacteriology: A Manual of Lecture Notes, (1950), unpublished.

‖ References 27 and 28.

¶ References 23 and 27.

Bacteriology

With the exceptions to be noted, infecting organisms were identified as Clostridium perfringens, either as pure culture or as mixed with other anaerobic and/or aerobic cocci

Reported Cases of Gas Gangrene Panophthalmitis

Author	Reference	Date of Report	No. Reported	Comment
Chuillous	1	1904	1	*
	2	1905	1	
Darier	3	1905	1	*
	4	1906	1	
Benedetti	5	1907	1	*
Hanke & Tertsch	6	1907	1	*
Schumacher	7	1908	1	
James	8	1910	1	
	9	1910	1	
Lutz	10	1910	3	*
Oreste	11	1910	1	
Heath	12	1929	1	*; AT †
Ridley	13	1929	1	AT
Hamilton	14	1930	2	AT
Beery	15	1932	1	
Walker	16	1934	1	AT
Klüver & O'Brien	17	1936	1	*; AT; ‡
Rieger	18	1936	1	
	19	1937	5	§
Canon	20	1938	6	§
Walker	21	1938	1	AT
Cross	22	1941	12	AT (in 10)
Davidson & Burn	23	1944	1	*
Capus	24	1946	1	*; AT; P ‖; S ¶
Schreck	25	1949	1	AT; P; S
Stuart	26	1949	1	P
Janttil	27	1950	1	*; P; S
Thygeson ⁂	..	?	1	AT
Kennedy & Vogel	28	1951	3	AT; P
Rieger	29	1952	1	P; S

* Exceptional in some respect, referred to in text.
† AT: Patient given anti-gas-gangrene serum.
‡ Typhoid vaccine administered.
§ Milk injections administered.
‖ P: Penicillin administered.
¶ S: One of sulfonamides administered.
⁂ Thygeson, P.: Ocular Bacteriology: A Manual of Lecture Notes, 1950, unpublished.

and bacilli. Chaillous # was the first to identify specifically the organism of C. perfringens by means of morphological, cultural, and physiological characteristics. Darier * identified the infecting organism as C. perfringens, but by smear examination only. Hanke and Tertsch,[8] and Lutz [10] defined the infecting organisms only as Gram-positive, gas-producing, anaerobic bacilli, the latter author noting sporulation as well.

Beneditti [5] presented a case in which, previous to the panophthalmitis following perforating injury, he had isolated C. perfringens from the exudate of the homolateral chronically infected tear sac. Cross [22] felt that organisms producing gas gangrene could be found on the foreign body causing the injury, in the tear sac, in the conjunctival cul-de-sac, or on the lashes.

REPORT OF NEW CASES

Case 1.—*History.*—N. F., a 15-year-old white youth, was admitted to the Infirmary at 5 p. m. on Aug. 3, 1943. Thirty hours prior to admission, while hammering on a cold chisel, he felt something strike his right eye but had no further sensation of a foreign body or irritation until 12 hours later, at which time the eye started to pain and nausea commenced.

Past History and Physical Examination.—Not contributory.

Ocular Examination on Admission.—O. S.: normal. O. D.: faulty light projection. A frank panophthalmitis was present with chemosis and marked, mixed, circumcorneal congestion. An hypopyon half filled the anterior chamber. There was no light reflex from the fundus. The lids were swollen and edematous. An x-ray revealed a foreign body 1×1×1 mm. in the midvitreous.

Course in Hospital.—Oral sulfadiazine, 4.0 gm., was started shortly after admission, and four-hourly administration of 1.0 gm. continued for 10 days. Five hours after admission an intraocular metallic foreign body was surgically removed without difficulty through a small limbal incision by means of the giant magnet.

On the second postoperative morning there was no light perception O. D. There was a marked increase in lid edema, a ring abscess of the cornea, and the anterior chamber was filled with exudate. Systemic reaction was minimal. The eyeball was eviscerated.

Recovery was essentially uneventful, and the patient was discharged, with little or no drainage from the scleral sac, on Aug. 20.

Laboratory Studies.—W. B. C.: 15,000 on admission; 18,250 the following day; 13,500 ten days later.

Cultures: The intraocular metallic foreign body removed the day of admission showed no growth; the intraocular contents removed at evisceration was reported as "pure B. welchii"; draining exudate from conjunctival cul-de-sac and scleral shell showed no growth two days and five days after evisceration.

Case 2.—*History.*—W. A., a 9½-year-old white boy, was admitted to the Infirmary at 7:30 p. m., May 17, 1953, one hour after being struck in the right eye by a piece of wire which had been picked from the ground and thrown by a playmate. The wire was 2 mm.×30 cm., dirty, and rusted. The boy knew his eye was injured because of momentary slight pain, blood-tinged tears, and immediate, almost total, loss of vision.

Past History and Physical Examination.—Not contributory.

Ocular Examination on Admission.—O. S.: 20/70; with correction, 20/25+; normal in all respects. O. D.: shadows only, with faulty light projection. There was a dirty, ragged, slightly gaping perforation of the globe located at the limbus, extending from 9:30 to 11:00 o'clock. Prolapsed uveal tissue and vitreous filled the wound. There was subconjunctival and anterior chamber hemorrhage. An hyphema filled the lower third of the deep anterior chamber. Above the hyphema the anterior chamber was filled with stringy opacities. The lens was poorly seen, but appeared to be displaced backward and downward. There was no red reflex. The iris was caught in the wound from 8:00 to 10:00 o'clock. The extraocular movements were full. X-rays negative for opaque foreign body.

One and a half hours after the injury, aqueous penicillin (crystalline penicillin G), 200,000 units, was administered intramuscularly.

Course in Hospital.—Surgical repair was undertaken three and a half hours after admission and included débridement, amputation of prolapsed uveal tissue, and suture of wound edges, with inclusion of conjunctival edge in suture, forming a small limbal flap. An air bubble was placed in the anterior chamber. Ten per cent sulfacetamide ointment was applied to the conjunctival sac. Aqueous penicillin, 100,000 units, was given intramuscularly and ordered for every six hours.

On the second postoperative morning there were no significant systemic reactions, despite the severe local process. The right eye was proptosed 3 mm. Edema of the lids was extreme, but no palpable

References 1 and 2.

* References 3 and 4.

crepitus was noted. The conjunctiva was blanched and chemotic. The anterior chamber was filled with purulent exudate. Creamy exudate was oozing from beneath the edge of the sutured flap. On clinical evidence, a presumptive diagnosis of gas gangrene panophthalmitis was made. Antibiotic dosages were increased—aqueous penicillin, 1,000,000 units every two hours intramuscularly, and streptomycin, 0.25 gm. every six hours intramuscularly, such dosages being initiated 40 hours after the injury. Anti-gas-gangrene serum considered for treatment but decision made against its administration.

Seventy-two hours after the injury the right eyeball was enucleated. There was no frank bleeding at any time. There was coffee-colored discharge in the subconjunctival tissues and a gush of purulent exudate from the retrobulbar area. All the tissues were turgid with edema and emphysema, Tenon's capsule being 15-20 times normal thickness. The socket was irrigated with 10 cc. of aqueous penicillin, 500,000 units per cubic centimeter, and then packed loosely with petrolatum (Vaseline) gauze. The patient tolerated the surgical procedure well. Postoperatively, the intramuscular penicillin was continued, the streptomycin discontinued.

The postoperative course was generally uneventful, the drainage gradually diminishing until the patient was discharged, on June 8, 1953.

A temporary prosthesis was well tolerated a few days later. Healing was complete one month later, with appearance and function of the permanent prosthesis about the same as that seen in an aseptic enucleation case.

Laboratory Studies.—W.B.C.: Twenty-four hours after injury, 29,400; 72 hours after injury, 20,000; 96 hours after injury, 10,400.

Urine: A +1 sugar reaction 72 hours after injury. Other specimens all normal.

Cultures: From initial repair, no growth; of purulent conjunctival exudate 36 hours later, "mixed B. welchii and E. coli"; of retrobulbar exudate and intraocular exudate at time of enucleation, "pure B. welchii"; of secretions and from socket itself two days after enucleation and on several subsequent days, no growth.

Pathological Study.—Gross Examination of Enucleated Globe: Volume 6 cc.; weight 5.3 gm. The globe was distorted with an equatorial, superotemporal bulge. A perforation of the limbus was present. The anterior chamber was filled with purulent exudate. The pupil was 3 mm. The sclera was markedly injected, the optic nerve retracted.

The eye was opened horizontally. No lens was seen. Posterior chamber and vitreous cavity filled with white exudate. Total retinal detachment present, with underlying tannish-colored coagulum.

Microscopic Examination: Every layer of the ocular tissues was infiltrated with polymorphonuclear leucocytes. Lymphocytes were present in less degree.

The corneal epithelium was absent. The stroma was packed with polymorphonuclear leucocytes and lymphocytes; chain bacilli and long chains of cocci were profusely present in the perforation.

Both chambers and the trabeculum were packed with cells of acute inflammation, hemorrhage, and fibrin. The iris was moderately infiltrated.

The lens was practically dissolved away; the epithelium was gone and the anterior capsule partially absent. A small section of necrotic cortex was noted, and what else was left of the lens material was filled with acute inflammatory cells.

The choroid was 20 times normal width, being swollen with equal amounts of polymorphonuclear leucocytes, lymphocytes, hemorrhage, and fibrin. There were many areas of separation of the pigment epithelium of the retina from Bruch's membrane, and both structures showed areas of necrosis and disintegration.

The retina was mostly dissolved; the recognizable areas left were heavily infected with bacilli and coccoid chains.

The sclera was four times normal width, showing pronounced vascular congestion with polymorphonuclear cell margination.

The vitreous cavity was three-fourths filled with inflammatory cells, coagulum, hemorrhage, and bacteria.

Pathological Diagnosis.—Perforating wound at the limbus; acute purulent panophthalmitis, due to C. welchii; absence of most of lens and retina due to necrosis; surgical iridectomy; vitreous abscess.

Case 3.—M. M., a 27-year-old white man, was admitted to the Infirmary 10 p.m., July 14, 1953. He thought a foreign body might have struck his left eye while he was hammering on a piece of metal 24 hours previously. After the incident the patient felt no pain nor discomfort, and vision was not impaired. He was seen, however, shortly afterward by a doctor, who noted no serious injury, and no treatment was prescribed. Fourteen hours after injury the patient himself noted that vision in the left eye had decreased to finger counting at 3 ft., and the eye was starting to pain. These symptoms rapidly increased in severity up to the time of admission.

Past History and Physical Examination.—Not contributory.

Ocular Examination on Admission.—O. D.: 20/15; eye normal. O. S.: Light perception only, with inaccurate projection. Tenderness and swelling of lids. Intense ciliary and superficial congestion. Cornea and anterior chamber hazy; latter filled with fibrin and cells. Corneal surface smooth; subconjunctival hemorrhages inferotemporally, but no break visible in cornea or conjunctiva by slit-lamp

examination. Pupil 3 mm. and fixed. No red reflex. Schiøtz tensions: O. D. 17 mm; O. S. 30 mm.

Course in Hospital.—One hour after admission the patient received 200,000 units of aqueous penicillin with 600,000 units of penicillin G procaine administered intramuscularly. Topical drops of 2.5% chloramphenicol given and ordered for every hour thereafter. The morning following admission an x-ray showed an intraocular opacity in the lower anterior vitreous, 1×1×1 mm. in size. This was surgically removed, with difficulty, through the anterior chamber and a small limbal keratome incision, by means of the giant magnet. Aqueous penicillin, 1,000,000 units, with streptomycin, 0.5 gm., was given intramuscularly postoperatively, and half that dose ordered for every six hours thereafter. Sulfisoxazole (Gantrisin), 2.0 gm. given orally, and 1.0 gm. ordered to be given every four hours thereafter. By evening following this surgery there was a frank purulent panophthalmitis with hypopyon, chemosis, and proptosis. Pain was severe, with the globe stony-hard. Aqueous penicillin, 100,000 units, injected subconjunctivally.

On the second postoperative day the anterior chamber was filled with purulent exudate, the proptosis increased, and the globe remained stony-hard and was then immobilized. The left eyeball was eviscerated. Streptomycin was discontinued postoperatively and penicillin dosage increased to 1,000,000 units every four hours.

The postevisceration recovery was clinically uneventful, and the patient was discharged from the hospital on July 31.

One month later the socket was clean with good movement of the scleral shell, and the patient was fitted for a prosthesis with excellent results.

Laboratory Studies.—Urine: Admitting specimen gave sugar reaction +2, albumin +1; subsequent tests normal.

Cultures: Cultures of foreign body, of ocular contents from evisceration, and of secretions from scleral socket two and four days after evisceration reported as "pure B. welchii"; of conjunctival sac prior to evisceration, and of secretion from scleral shell six and eight days after evisceration showed no growth.

Case 4 (not panophthalmitis; included because of its relevant interest).—J. S., a 24-year-old white man, was admitted to the Infirmary at 7 p. m., April 5, 1954, seven hours after being struck in the left eye by a steel chip from a wedge being driven into a log by a fellow workman. There was immediate loss of vision in the injured eye. Two and a half hours after the injury the patient had received 400,000 units of penicillin and 0.5 gm. of streptomycin.

Past History and Physical Examination.—Not contributory.

Ocular Examination on Admission.—O. D.: Normal. O. S.: Light perception, with faulty light projection. There was a laceration of the left lower lid. A 2 cm. perforating wound of the globe was located midway between the insertions of the inferior and medial rectus muscles and extended across the sclera into the cornea. Uveal tissue prolapsed into the wound. Intraocular hemorrhage was apparent. The globe was mushy soft.

Course in Hospital.—An x-ray revealed an intraocular metallic foreign body, which was surgically removed the evening of admission. Postoperatively, penicillin, 1,000,000 units, with streptomycin, 0.25 gm., given intramuscularly every eight hours for 48 hours.

Postoperatively the left eye showed no evidence of inflammation of infectious origin; but there was no light perception present in the destroyed globe, so that it was enucleated on the third day following the initial foreign body removal.

Healing and recovery were uneventful.

Laboratory Studies.—Cultures: Cultures of intraocular foreign body, "pure B. welchii"; of secretions in cul-de-sac subsequently, no growth.

BACTERIOLOGY

Terminology.—In this report (except, of course, when referring directly to laboratory reports or previous papers) the nomenclature of Bergey is used,[30] which is the preferred usage as defined in the A. M. A. "Standard Nomenclature of Diseases and Operations."[31]

Clinical Pathology and Bacteriology.—Gas gangrene, as seen in wounds generally, is an infection caused by one or more of a group of soil anaerobes which are ubiquitous in distribution.† Four species of the genus Clostridium have been identified with cases of gas gangrene seen in humans, all anaerobic, sporulating, Gram-positive rods which produce powerful exotoxins and may be considered as potential etiologic agents in gas gangrene panophthalmitis.

Clostridium perfringens (common name Bacillus welchii; also called B. aerogenes capsulatus, B. phlegmonis emphysematosae, Frankel-Welch bacillus, Clostridium welchii, B. perfringens, B. enteriditus-sporogenes) has been identified in the large majority of war wounds with mixed anaerobic flora

† References 32 through 36.

(approximately 75%)[32] and so frequently in panophthalmitis that "B. welchii panophthalmitis" is a term in common usage. Clinical characteristics, when the organism is found in pure culture (about 70%), are marked tissue emphysema, produced by fermentation of muscle sugars, and necrosis and hemolysis, caused by the formation of specific exotoxins.

Clostridium novyi (common name Bacillus œdematiens; also called Clostridium œdematiens) was seen in about 30% of the war wounds with mixed anaerobic flora.[32] When identified as the sole cause of infection (about 12%), the feature is extreme edema. Emphysema, necrosis, and hemolysis are not predominant.

Clostridium septicum (common name Vibrion septique; also called B. septicus, Clostridium œdematis-maligni, B. œdematis-maligni, and bacillus of "malignant edema") was isolated in about 10-12% of the war wounds with mixed flora, but has rarely been found in pure culture in human wounds. (This organism is identified not uncommonly in veterinary bacteriology, with the fatal "malignant edema.") When it is found as the important factor in human gas gangrene, edema and blood-stained fluid are predominant features, with necrosis and emphysema present but secondary in clinical importance.

Clostridium histolyticum (also called B. histolyticus) was the organism found most rarely in the war wound infections (6%). It has never been found as the sole pathogen. In laboratory animals an extremely destructive local process of necrosis and digestion of tissue is characteristic, with very little systemic reaction. This organism differs from the first three in being primarily proteolytic rather than saccharolytic. Hydrogen sulfide is released, but there is no tissue fermentation, i. e., gas formation, and hemolysis is not apparent.

Identification of the Organism.—There are a multitude of minute morphological, cultural, and physiological variations present among these species of Clostridium that will not be dealt with. The significant factors are as follows: 1. All but C. histolyticum are obligate anaerobes, but all will show growth in the usual laboratory media, such as gelatin or blood agar stabs, meat broths, etc., which are not under strictly anaerobic conditions. 2. All but C. histolyticum will show at least some formation of acid and gas. 3. All four species will liquefy gelatin and cause hemolysis of blood agar to a recognizable degree.

Differentiation of the species of Clostridium present may be made by subculture into an iron-milk medium and anaerobic incubation. Characteristics are as follows: (1) C. perfringens—early (10-24 hours), very singular violent gaseous fermentation with coagulation of the medium, but no blackening or digestion; (2) C. novyi—inactive gaseous fermentation, long continued, no coagulation (or very late), no blackening or digestion; (3) C. septicum—moderate gaseous fermentation, coagulation usually present, no digestion or blackening, and (4) C. histolyticum—no gaseous fermentation, usual early blackening (24-48 hours), digestion of medium with or without previous clotting.

Inoculation into laboratory animals is definitive but usually unnecessary, the clinical course of the disease in the patient being far ahead of the laboratory study, and the diagnosis apparent. Further, since the antitoxic serum commonly used for therapy is polyvalent, identification of individual pathogenic species of anaerobes may at times appear to be of academic value.

COMMENT

The relative rarity of gas gangrene in wounds generally, and in panophthalmitis specifically, is not completely understood. Pathogenic anaerobes are not uncommonly found on routine bacteriological examination in the absence of clinical disease.‡ It has been shown in laboratory animals§ that inoculation of anaerobic pathogens directly into the lens or vitreous is necessary to produce panophthalmitis, but this specification

‡ References 32 through 36. Case 4.

§ References 37 through 39.

is met often enough clinically. The great majority of cases in this series of perforating injuries was consequent to insult by relatively low-velocity missiles; but some were of war injuries subsequent to explosions,‖ and presumably the perforating missiles were traveling at high velocity. The latter certainly were not sterile, an idea which is being less commonly accepted than heretofore.[40]

It is possible that some sort of symbiotic relationship of one of the pathogenic anaerobes with one or more of the same group, or with a saprophytic organism, is necessary in order to initiate this virulent process. Most of the laboratory reports were labeled "pure cultures of B. welchii"; but consideration of the laboratory conditions under which the cultures were grown, and the peculiarly overwhelming characteristics of C. perfringens might well lead to the fair conclusion that other organisms were present but had not had the opportunity to demonstrate growth.

In reviewing cases through 1936, Duke-Elder placed gas gangrene panophthalmitis in a class by itself,[41] and summarized the typical symptoms and signs: (1) pain greater than usual; (2) intraocular tension rise early; (3) coffee-colored discharge, and (4) gas bubble in the anterior chamber. The last two signs were emphasized as characteristic. Two-thirds of all the reported infections have occurred since 1936, and the significance of these signs has been reaffirmed. Clinical appearance has been entirely consistent with the known characteristics demonstrated by the anaerobic pathogens under consideration. Pain, presumably the consequence of rapid rise in intraocular tension, was more pronounced when drainage was impossible or inadequate through the perforating wound. The coffee-colored discharge, dependent on the amount of hemolytic activity, was of variable degree, as was the presence of gas bubbles in the anterior chamber. Rapid loss of vision progressive to total amaurosis is so unusual a feature and appeared so consistently in this series that its inclusion as a characteristic sign should not be overlooked. This total loss of light perception could well be due to the actual destruction of the neurovisual elements by specific necrolyzing exotoxins. Additional damage is caused by the mechanical and physical factors of tearing and splitting of the neuroretinal layers by gas formation. All those features were clearly apparent in the pathological sections of the globe reported in Case 2.

Conventional prophylactic measures have been entirely impotent against this disastrous disease process, even though some cases were seen very early.¶ Everything conceivable, with the exception of intravitreal or subconjunctival prophylactic injection, was attempted. In laboratory animals, any treatment, including intraocular injections of antibiotics, has been of little value if more than three hours have elapsed since the inoculation of gas gangrene organisms into the lens or vitreous.[37] Penicillin offers the best therapeutic agent available at this time,# but systemic administration of the drug, at best, has been shown ineffectual against intraocular infections. The administration of antitoxin in therapeutic doses had no demonstrable beneficial effect on the course of the panophthalmitis and did not aid in the recovery to any perceptible degree. Therapeutic dosage of anti-gas-gangrene serum sufficient to be of conceivable aid is not without considerable danger, and it is suggested that this type of therapy might well be reserved for the possible cases[23] which do not respond well to surgical intervention. It would be more apropos to administer as a routine the commercially available combined tetanus antitoxin-gas gangrene antitoxin as a prophylactic measure in perforating wounds, rather than the tetanus antitoxin alone, the latter being commonly done in many areas.

The choice of enucleation or evisceration seems to have made little difference in this series, but if retrobulbar infection is suspected, enucleation would be preferred.

‖ References 23 and 24.

¶ Case 2. References 23 and 24.

References 37 through 39, 42.

SUMMARY

1. Fifty-three cases of gas gangrene panophthalmitis reported in the literature are briefly reviewed. Three are added to the seven reported from the United States.

2. The clinical course of the disease, with the main characteristics of the organisms potentially capable of causing such course, are discussed.

3. The correlation of variable symptomatology with the pathogenic process is pointed out. It is suggested that rapid loss of vision to total blindness is a characteristic sign.

4. The fact that all types of treatment attempted (other than surgical) have been ineffectual is noted, and the use of antitoxin as a therapeutic measure with its potential danger, but without demonstrable benefit, is questioned.

5. Enucleation is proposed as the operation of choice if retrobulbar infection is suspected.

REFERENCES

1. Chaillous, J.: Infection traumatique du globe oculaire par un microbe anaerobie (Bacillus perfringens), Rec. opht. **26**:678, 1904.

2. Chaillous, J.: Deux cas d'infection traumatique de globe oculaire par un microbe anaerobie (Bacillus perfringens), Ann. ocul. **134**:115, 1905.

3. Darier, A.: Panoptalmie et Bacillus perfringens, Clin. opht. **11**:*266*, 1905.

4. Darier, A.: Panoptalmie gazeuse et Bacillus perfringens, Clin. opht. **12**:*227*, 1906.

5. Beneditti, A.: Panoftalmitis da Bacillo perfringens, Clin. ocul., Palermo **8**:3013, 1907.

6. Hanke, V., and Tertsch, R.: Einige seltene Infektionen des Auges, Klin. Monatsbl. Augenh. **45**:545, 1907.

7. Schumacher, G.: Anaerobe Bazillen bei Augenverletzungen, Klin. Monatsbl. Augenh. **46**: 34, 1908.

8. James, R. R.: Contribution to the Bacteriology of Panophthalmitis, Tr. Ophth. Soc. U. Kingdom **30**:179, 1910.

9. James, R. R.: Penetrating Injury of the Globe with Panophthalmitis Due to a Gas Forming Micro-Organism, Ophth. Rev. **29**:161, 1910.

10. Lutz, A.: Über einige Fälle von ektogener Panophthalmie (Infektionen mit Pneumococcus subtilis und Anaerobionten), Klin. Monatsbl. Augenh. **48**:31, 1910.

11. Oreste: Plaie pénétrante de globe par coup de Fouet (Infection par le Bacillus perfringens), Ann. ocul. **143**:35, 1910.

12. Heath, W. E.: Bacillus Welchii Infection of Globe, Brit. J. Ophth. **13**:574, 1929.

13. Ridley, F.: Gas Gangrene Panophthalmitis, Tr. Ophth. Soc. U. Kingdom **49**:221, 1929.

14. Hamilton, J. B.: Notes on B. Welchii Infection of the Globe, Brit. J. Ophth. **14**:452, 1930.

15. Beery, E. B.: Intra-Ocular Foreign Body with Bacillus Welchii Infection, Am. J. Ophth. **15**:1022, 1932.

16. Walker, S., Jr.: Bacillus Welchii Panophthalmitis, J. A. M. A. **102**:1561, 1934.

17. Kluver, H. C., and O'Brien, C. S.: Panophthalmitis Due to Clostridium Welchii, Arch. Ophth. **15**:1088, 1936.

18. Rieger, H.: Wundinfektion des Augapfels mit Bazillen der Gasbrandgruppe, Klin. Monatsbl. Augenh. **96**:548, 1936.

19. Rieger, H.: Über Wundinfektion des Augapfels mit Erregern der Gasbrandgruppe, von Graefes Arch. Ophth. **137**:61, 1937.

20. Canon, G.: Der Gasbrand am menschlichen Auge, Klin. Monatsbl. Augenh. **100**:394, 1938.

21. Walker, S., Jr.: Prognosis of Bacillus Welchii Panophthalmitis, Arch. Ophth. **19**:406, 1938.

22. Cross, A. G.: Gas Gangrene of the Eye, Lancet **2**:515, 1941.

23. Davidson, W. G., and Burn, J. K. A.: Gas Gangrene Infection of the Eye and Orbit, Tr. Ophth. Soc. U. Kingdom **63**:375, 1944.

24. Capus, B.: Clostridium Welchii Panophthalmitis: Report of a Case, Arch. Ophth. **36**: 226, 1946.

25. Schreck, E.: Gasbrand und Auge, Klin. Monatsbl. Augenh. **114**:364, 1949.

26. Stuart, J.: Clostridium Welchii Infection of the Eyes, Brit. M. J. **1**:272, 1949.

27. Janttii, K.: Panophthalmitis Due to Clostridium Welchii, Duodecim **66**:676, 1950.

28. Kennedy, R. J., and Vogel, A. W.: Intraocular Infection with the Gas-Forming Bacillus Clostridium Welchii: Report of a Case, A. M. A. Arch. Ophth. **45**:528, 1951.

29. Rieger, H.: Zur Gasbrandinfektion des Augapfels, Wien. med. Wchnschr. **102**:31, 634, 1952.

30. Bergey, D. H.: Bergey's Manual of Determinative Bacteriology, Sixth Edition, Baltimore, Williams & Wilkins Company, 1948, pp. 743-790.

31. Plunkett, R. J., and Hayden, A. C., Editors: Standard Nomenclature of Diseases and Operations, Published for the American Medical Asso-

ciation, Fourth Edition, New York, Garden City, N. J., 1952, p. 52.

32. Weinberg, M., and Seguin, P.: La gangrène gazeuse, Paris, Masson & Cie, 1918.

33. Smith, D. T., and Martin, D. S.: Zinsser's Textbook of Bacteriology, Ninth Edition, New York, Appleton-Century-Crofts, 1948, pp. 431-492.

34. Jordan, E. O., and Burrows, W.: Jordan-Burrows Textbook of Bacteriology, Fifteenth Edition, Philadelphia, W. B. Saunders Company, 1949, pp. 22-23 and 566-598.

35. Bryan, A. H., and Bryan, C. G.: Principles and Practice of Bacteriology, Fourth Edition, New York, Barnes & Noble, Inc., 1951, pp. 175-177 and 258-261.

36. Altemeier, W. A., and Gibbs, E. W.: Bacterial Flora of Fresh Accidental Wounds, Surg., Gynec. & Obst. **78**:164, 1944.

37. von Sallmann, L.: Penicillin and Sulfadiazine in the Treatment of Experimental Intraocular Infections with Staphylococcus Aureus and Clostridium Welchii, Arch. Ophth. **31**:54, 1944.

38. von Sallmann, L.: Penetration of Penicillin into Eye: Further Studies, Arch. Ophth. **34**:195-201, 1945.

39. Hoskins, L. D.: Penicillin Therapy of Experimental Infections of the Lens and Vitreous with Clostridium Welchii, Arch. Ophth. **38**:301, 1947.

40. Cross, G. H.: Injuries of the Eye, in the Eye and Its Diseases, Second Edition, Edited by Conrad Berens, Philadelphia, W. B. Saunders Company, 1949, p. 783.

41. Duke-Elder, W. S.: Text-Book of Ophthalmology, Vol. III, St. Louis, C. V. Mosby Company, 1941, pp. 2221-2225.

42. Leopold, I. H.: Surgery of Ocular Trauma, A. M. A. Arch. Ophth. **48**:378, 1952.

News and Comment

GENERAL NEWS

Committee on Illustrations, Pan-American Ophthalmological Association.—The Committee on Illustrations of the Pan-American Ophthalmological Association is attempting to develop a library of slides and movies on ophthalmic subjects for interchange among the members in the countries of the Americas for teaching purposes. At this time an invitation is being tendered to those who are interested in donating any suitable material. We have already received several sets of slides and have been promised others.

Dr. Moacyr Alvaro, our President, will receive any such material from members south of Panama. His address is Consolacao 1151, São Paulo, Brazil. Material from members in the northern countries should be sent to the Committee chairman, Dr. Saul Sugar, 18140 San Juan Drive, Detroit 21. Each donor will receive a letter and receipt, which can be used for deducting the value of the donation from income taxes.

Two distributing points will be designated by the Pan-American Association at a later date.

Leiomyoma of the Iris

Report of a Case and Review of Literature

LT. WAYNE L. ERDBRINK (MC), U. S. N.
and
CAPT. FRED HARBERT (MC), U. S. N. (Ret.)

Tumors of the iris arising from the sphincter and dilator muscles are rare, and most authors concerned with the subject agree with Duke-Elder's [5] statement that these tumors are impossible to diagnose clinically and their pathological recognition is by no means easy. Friedenwald and associates [11] and Berliner [3] state that they are clinically indistinguishable from malignant melanoma, especially those which are lightly pigmented.

In 1923, Li [17] found only 6 iris tumors in 154 cases of tumor of the uveal tract examined microscopically at the Massachussetts Eye and Ear Infirmary from 1900 to 1922. Two of these tumors were leiomyomas of the iris. Ferrer,[9] in 1949, studied five leiomyomas from the Institute of Ophthalmology of the Presbyterian Hospital of New York. Leiomyomas constituted about 9% of the 58 iris neoplasms, or about 2% of the uveal tract neoplasms in her series. Heath,[14] in 1951, collected and reviewed 19 specimens of iris muscle tumors from the Massachusetts Eye and Ear Infirmary and from the Armed Forces Museum of Pathology and found that tumors of the iris muscles constitute only about 4% of all primary and secondary iris neoplasms. These studies indicate the rarity of leiomyoma of the iris.

A case of this rare iris tumor is here reported, with a review of the literature on the subject. The following case is the 20th individual case to be reported in the literature of a tumor purporting to be a leiomyoma of the iris and is the first such case subjected to radioactive phosphorus (P^{32}) uptake studies prior to surgical removal.

From the Ophthalmology Service, U. S. Naval Hospital, Philadelphia.

Presented before the College of Physicians of Philadelphia, Section on Ophthalmology, Dec. 16, 1954.

REPORT OF CASE

J. L. McD., a 20-year-old white seaman, was admitted to the U. S. Naval Hospital, Philadelphia, on Jan. 28, 1954, with a "spot" on the iris of the left eye. This "spot" seemed to be stationary during the 17 to 18 months since it had first been noted. The vision was 20/20 in each eye with correction. A 40 Δ comitant, alternating esotropia at distance and near was present and was not affected by lenses. This esotropia dated from early childhood. At 7 o'clock on the blue iris of the left eye there was a well-circumscribed, salmon-colored tumor, 3 mm. in diameter, which was in contact with the corneal endothelium and which projected somewhat into the pupillary space. The pupil dilated well and symmetrically, causing the tumor to project into the pupillary area to a greater extent. Schiøtz tensions were normal in both eyes. Gonioscopy revealed a free angle, but four to five moderate-sized blood vessels ran from the irregular, glossy surface of the tumor into the angle. Slit-lamp examination revealed the salmon color to be due to vessels in the otherwise unpigmented tumor. Complete laboratory and x-ray studies were within normal limits (Fig. 1).

On Jan. 28, 1954, the patient was presented at the clinic of Dr. Francis Heed Adler, Hospital of the University of Pennsylvania. Dr. Adler and staff concurred in our clinical impression of leucosarcoma, or nonpigmented melanoma of the iris, and recommended excisional biopsy of the tumor.

On Feb. 4 radioactive phosphorus (P^{32}) uptake studies were performed by Dr. I. J. Eisenberg in the Isotopes Department, Wills Eye Hospital, Philadelphia. One-hour and 24-hour uptake readings were taken, and no abnormal uptake of P^{32} was reported. This was interpreted as evidence of a nonmalignant growth.[7]

On Feb. 9, excisional biopsy was performed by a basal iridectomy in the inferior nasal quadrant of the left eye. There was no hemorrhage, and the postoperative course was uneventful (Fig. 2).

At the annual Wills Eye Hospital Conference, on Feb. 20, 1954, the hematoxylin-eosin-stained sec-

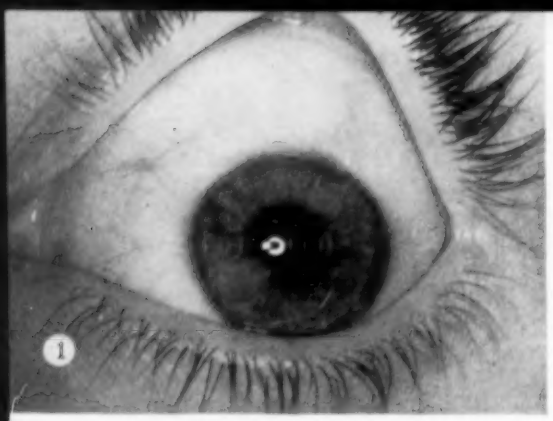


Fig. 1.—Tumor of the iris, inferior nasal quadrant of the left eye.

tions of the tumor were reviewed by Drs. F. H. Verhoeff and Parker Heath, of Boston, and J. S. McGavic, of Philadelphia, who agreed that this tumor was a leiomyoma of the iris. The following is the pathologic report of Dr. J. S. McGavic: "This tumor of the iris shows a leiomyoma. I am unable to tell whether or not it arose from the dilator or sphincter muscle of the iris, but I believe the tumor is benign. The diagnosis could be made almost certain with the hematoxylin and eosin stain, but the Mallory phosphotungstic [acid] stain showed the myoglial fibers to my satisfaction." Figure 3 illustrates the typical arrangement of the spindle cells with the variation in the size and staining properties of the individual cells, along with the vascularity of the surface of the tumor. Figure 4 shows the spindle shape of the cells with the long tapering processes at the ends of the cells.

On Aug. 25 and Dec. 1, 1954, the patient was re-examined at the U. S. Naval Hospital, Chelsea, Mass., by Cmdr. D. A. Mills (MC), U. S. N., and the eye operated on was found to have 20/20 vision with correction, normal intraocular tension, an open angle, and no evidence of recurrence of the tumor.

In 1923, Verhoeff [28] reported a case of leiomyoma of the iris that was most unusual in that from 1904 to 1920 three surgical procedures were performed for removal of the tumor prior to eventual enucleation of the eye. This case was followed over a 19-year-period, and Verhoeff was convinced that the neoplasm was nonmalignant. With the publication of this case, Verhoeff established the pathologic criteria for a diagnosis of leiomyoma of the iris. These, as stated by Reese,[21] are (*a*) a structure of interlacing, closely packed bundles of elongated, spindle-shaped cells; (*b*) long oval nuclei, tending to arrange themselves in a palisade formation; (*c*) granular eosinophilic cytoplasm of the cells, and (*d*) the demonstration of myoglia fibrils with the Mallory phosphotungstic-acid hematoxylin, Masson trichrome, or gold impregnation stain. Verhoeff also pointed out that myoma cells are truly spindle-shaped, whereas the cells of uveal spindle-cell melanomata are seldom, if ever, distinctly spindle-shaped, but terminate in or send off laterally several ill-defined, irregular processes, which anastomose with neighboring cells to form a more definite syncytium. Griffith, in his pathologic report for Thompson [25] in 1899, also made a point of this difference in cell shape between myoma and spindle-cell sarcoma.

Verhoeff's case was the first leiomyoma of the iris demonstrated by special stains. Reese [21] states that the demonstration of myoglia fibrils is the most important differential diagnostic point pathologically. Verhoeff states that he has never been able to find any myoglia fibrils in association with spindle-cell melanomata of the uvea.

Friedenwald and associates,[11] Heath,[14] and Ferrer [9] agree that no metastases from leiomyomata of the iris have occurred, and that these neoplasms are to be considered benign. However, it is possible that localized growth of the neoplasm may be associated with hyphema, cataract, and/or glaucoma.

Reese [21] states that smooth muscle from which a myoma may arise in the eye is mesodermal in origin in the ciliary body, orbit, and media of blood vessels. That the sphincter and dilator muscles of the iris are neuroectodermal in origin is well documented by Mann.[18] Smooth muscle tumors may arise, however, at sites where smooth muscle is

Fig. 2.—Postoperative appearance, basal iridectomy, inferior nasal quadrant, left eye.

not ordinarily found. Verhoeff [28] concluded that his case had originated from the stromal cells of the embryonic uvea, possibly from misplaced cells which ordinarily would have taken part in the formation of the ciliary muscle, thus being mesoblastic in origin. Heath [14] states that he has reviewed this material and restained it, and is of the opinion that it originated from the anchor tissue of the dilator muscle at its ciliary part, being thus epiblastic in origin. Reese states that he is unaware of any histologic differences in the tumors as a result of their site of origin. Friedenwald and associates [11] state that sphincter and dilator muscle tumors are true leiomyomas, indistinguishable histologically from smooth muscle tumors of mesodermal origin found elsewhere in the body.

Table 1 presents an abstract of the historical and clinical characteristics of the original publications of the 19 recorded cases found in the literature and of the case here reported.

Verhoeff [28] reviewed all published papers prior to 1923 reporting myomata of the iris and ciliary body and accepted only those cases described by Thompson [25] and van Duyse [26] as probable instances of true leiomyomata of the iris. He did not accept any of those reported as being myomata of the ciliary body. Blodi,[2] in 1950, has probably reported the only conclusive case of leiomyoma of the ciliary body found in the literature to date.

Davis and associates [8] state that personal communication with Zentmayer [30] indicates that the latter's case, originally published as a primary sarcoma of the iris (leucosarcoma), was found on reexamination to be a leiomyoma. Kirby [16] and the Moultons [19] refer to Davis' communication, but no subsequent report by Zentmayer appears in the literature.

Reese [21] seemingly has accepted the case reported by van Heuven,[27] but Blodi [2] and Ferrer [9] are of the opinion that the tumor in van Heuven's case is a questionable leiomyoma. This tumor was located in the superior temporal quadrant of the iris and is the second case report (Ferrer's Case 4) of a tumor located superiorly in the iris.

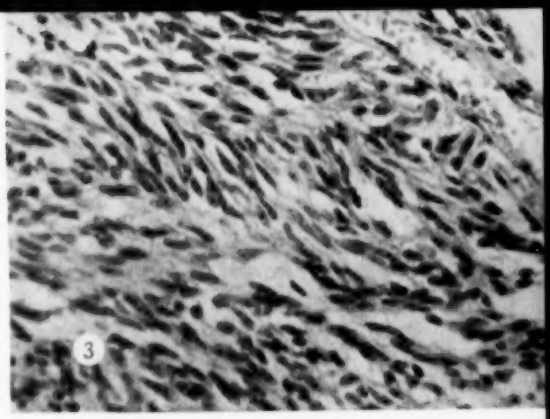


Fig. 3.—Photomicrograph; reduced to 76% of mag. × 200; hematoxylin and eosin.

In her excellent study, Ferrer [9] examined pathologically the case reported by Frost [12] and four other cases of her own (Table 1, Cases 2-5). Her Case 4 had an intraocular tension of 55 mm., but this was felt to be due to primary glaucoma and not to be associated with the tumor.

Fulgosi [13] reports an unusual case which had unbearable pain in the eye. The tumor was observed to increase in size, and it produced an irregular astigmatism from corneal pressure, thus greatly reducing vision. This case graphically illustrates how mechanical effects from this benign tumor will affect the eye and is the only case reported with associated ocular pain.

Table 2 summarizes the historical and clinical characteristics of the 20 cases of leiomyomata of the iris here reviewed.

Melanoma is the outstanding differential diagnostic problem, especially leucosarcoma, or nonpigmented melanoma, of the iris. Other possible conditions are intraepithelial and implantation cysts, inflammatory granuloma (gumma, tuberculoma, sarcoid), metastatic

Fig. 4.—Photomicrograph; reduced to 76% of mag. × 500; Mallory phosphotungstic-acid hematoxylin stain, showing the myoglia fibrils.

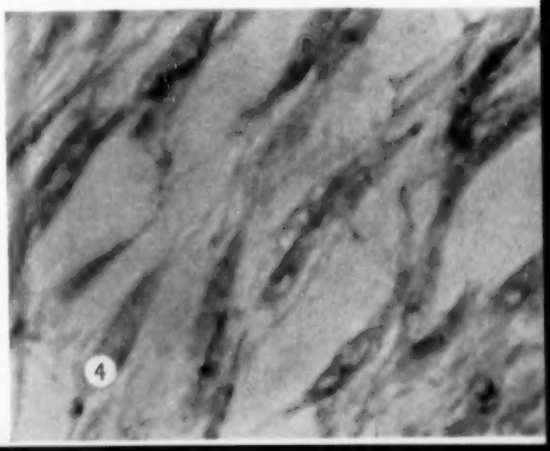


TABLE 1.—*Abstract of Reported Cases*

	Thompson 1866	van Duyse 1911	Verhoeff 1925	Zentmayer 1930	Frost 1937	Ellett 1939	van Heuven 1942	Kahler and others 1943	Davis and others 1944	Moulton and Moulton 1948
Age	51	28	33 (1904)	10	46	47	54	46	27	56
Sex	M	F	M	M	F	M	F	F	F	M
Eye	O. D.	O. D.	O. S.	O. S.	O. S.	O. D.	O. D.	O. D.	O. D.	O. D.
Site	Inferior temporal	Inferior temporal	Inferior temporal	Inferior temporal	Inferior temporal	Inferior nasal	Superior temporal	Lower quadrant	Inferior temporal	Inferior temporal
Duration	Unknown	20 yr.	Always	4 mo.	10 mo.	15-20 yr.	.....	2 yr.	Unknown	1½ yr.
Vision	6/9	1/1	20/20	5/5	20/20	20/15 cc.	Good	20/20 cc.	.....	4/200
Shape	Cauliflower	2 protuberances	Pupil to iris base	Ovoid	Nodular	Pupil to iris base	.....	Sessile; cystic	Nodular	Egg-shaped
Elevation	.....	1.5 mm.	Cornea	.....	1 mm.	.....	Flat	.....	3 mm.	.....
Size	3×4 mm.	2.5 mm.	4×5 mm.	3×5 mm.	Small	.....	.....	3 mm.	9×6 mm.	5×7 mm.
Pupil	Ectropion; reactile; tumor projected	Margin involved	.....	Reactile; tumor projected	Ectropion	Reactile	.....	Reactile	.....	Reactile
Color	Light brown	White	Pink	Pinkish	Yellow-gray	Semiclear, became dark	Pale; glassy	Grayish	Opaque	Salmon
Vascularity	Absent	Present	Present	Present	Present	Present	.....	Present	.....	Present
Angle	Free	Free	Free	Free	Free	Involved	Free	Free	.....	Involved
Tension	Normal	Normal	.....	.....	.....	Normal	.....	.....	.....	.....
Hyphema	.....	9 times	Recurrent	.....	.....	One (1)	.....	.....	.....	.....
Cataract	.....	.....	.....	.....	.....	Behind tumor	.....	.....	.....	Advanced
Origin	.....	.....	(?) Mesodermal	.....	(?) Sphincter	Epiblastic	Teratoid	Dilator	.....	.....
Surgery	Iridectomy	Iridectomy	Enucleation (1920)	Iridectomy x-ray	Enucleation	Enucleation	Enucleation	Iridectomy	Iridectomy	Enucleation
Follow-up	26 mo.*	8 mo.	19 yr.	3½ yr.	3 yr.†	10 mo.	4 yr. (?)	16 mo.	.....	.....

	Fleming 1948	O'Day 1949	Ferrer Case 2 1949	Ferrer Case 3 1949	Ferrer Case 4 1949	Ferrer Case 5 1949	Stanworth 1950	Kirby 1953	Fulgosi 1953	Erdbrink and Harbert 1954
Age	.....	65	51	48	28	17	58	.....	32	20
Sex	F	F	F	F	F	F	F	F	M	M
Eye	O. S.	O. D.	O. D.	O. D.	O. S.	O. D.	O. S.	O. S.	O. D.	O. S.
Site	Inferior nasal	Inferior temporal	Inferior nasal	Nine (9) o'clock	Superior temporal	Nine (9) o'clock	Inferior nasal	Inferior temporal	Nine (9) o'clock	Inferior nasal
Duration	1 yr.	1 yr.	Unknown	Unknown	Always	Unknown	1 day	(?) 5 yr.	7 mo.	17-18 mo.
Vision	6/5 cc.	6/36	6/200	20/20	H. M.	20/20	6/6	20/20	6/20	20/20 cc.
Shape	Bean-shaped	Sessile	.....	.....	.....	.....	.....	.....	Nodular	Nodular
Elevation	Cornea	.....	.....	.....	.....	.....	.....	1.5 mm.	Cornea	Cornea
Size	.....	Quadrant	.....	.....	.....	.....	2 mm.	.....	5.5 mm.	3 mm.
Pupil	Margin involved	Ectropion; reactile	Ectropion	Ectropion	Ectropion	Ectropion	Reactile; tumor projected	Flattened	Reactile; tumor projected	Reactile; tumor projected
Color	Purple-black	Gray	Some pigment	Rosy	Some pigment	Rosy	Light pigment	.....	Yellow-gray	Salmon
Vascularity	.....	Present	.....	.....	Present	.....	Present	Present	Present	Present
Angle	.....	Involved	Free	Free	Free	Free	Free	Free	.....	Free
Tension	.....	Normal	Normal	Normal	55	Normal	.....	.....	Normal	Normal
Hyphema	.....	.....	.....	.....	.....	.....	.....	.....	One (1)	None
Cataract	.....	Behind tumor	Advanced	.....	.....	.....	Behind tumor	.....	.....	None
Origin	(?) Dilator	.....	Dilator	.....	Sphincter	Sphincter	.....	(?) Dilator	(?) Dilator	Unknown
Surgery	Iridectomy	Enucleation	Iridectomy	Iridectomy	Enucleation	Enucleation	Iridectomy	Iridectomy	Enucleation	Iridectomy
Follow-up	3 yr.	.....	.....	.....	.....	.....	.....	7 yr.	.....	10 mo.

* Wood and Pusy.[29]
† Ellett.[5]

carcinoma, hyperplasia of the pigment epithelium, primary carcinoma of the pigment epithelium, encysted foreign body, lymphosarcoma, and broad anterior peripheral synechiae.

Duke-Elder and Stallard,[6] in 1930, reviewed all reported cases of leucosarcoma of the iris and contributed 1 case, making a total of 26 cases. This tumor entity was nodular in shape and was confined to the lower half of the iris, especially the inferior temporal quadrant. It is obvious that the clinical differentiation of leiomyoma and leucosarcoma of the iris would be most difficult.

TABLE 2.—*Historical and Clinical Characteristics in Twenty Cases* *

Race		
	Caucasion only reported	
Age		
(18)	10-20 yr.	2
	20-30	4
	30-40	2
	40-50	4
	50-60	5
	60-65	1
Sex		
(20)	F	13
	M	7
Eye		
(20)	O. D.	12
	O. S.	8
Site		
(20)	Inf. temp.	12
	Inf. nasal	5
	Sup. temp.	2
	Inf. quad.	1
Duration		
(19)	2 yr. or less	9
	Unknown	5
	Always present	2
	15-20 yr.	2
	5 yr.	1
Vision		
(19)	20/20 ±	14
	Poor—	
	Cataract	3
	Astigmatism	1
	Glaucoma	1
Shape		
(13)	Nodular, sessile, or circumscribed	11
Elevation		
(9)	Elevated	4
	Corneal contact	4
	Flat	1
Size		
(12)	Range in diameter 3-9 mm.	
Pupil		
(17)	Normal reactions	9
	Ectroplon uveae	7
	Tumor projected	5
	Margin involved	2
	Flattened	1
Color		
(19)	Pink	6
	Yellow-gray	4
	White	4
	Some pigment	4
	Black	1
Vascularity		
(14)	Present	13
	Absent	1
Angle		
(17)	Free	14
	Involved	3
Tension		
(10)	Normal	9
	Elevated	1
Hyphema		
(5)		
Cataract		
(5)	Behind tumor	3
Origin		
	???	
Surgery		
(20)	Iridectomy	11
	Enucleation	9
	X-ray	1)
Follow-up		
(11)	Range 8 mo. 19 yr.	
	No metastasis	

* Figure in parentheses is the number of cases reporting.

Recently Eisenberg and associates[7] have outlined the criteria for radioactive phosphorus (P^{32}) testing as an aid in differentiating malignant and nonmalignant intraocular neoplasms. It is our hope that other cases of leiomyoma of the iris can be subjected to P^{32} uptake studies in order to validate the findings of the case here reported.

In considering the proper management of leiomyoma of the iris, it would be well to think of iris melanoma at the same time. Of historical interest is the position taken by Wood and Pusey,[29] who, in 1902, emphatically stressed the necessity of enucleation in all cases of "primary sarcoma of the iris." Duke-Elder and Stallard,[6] in their discussion of leucosarcoma; Reese,[21] in his discussion of benign and malignant melanomata of the iris, and Kirby,[16] Sanders,[23] Heath,[14] Ferrer,[9] and Reese,[21] in discussing leiomyoma of the iris, all agree that excision is indicated when the tumor is sufficiently localized to permit complete excision, but that enucleation should be undertaken when there is active growth associated with diffuse involvement of the iris and/or the angle. O'Day[20] stated that every unpigmented or lightly pigmented tumor of the iris should be treated conservatively or subjected to biopsy before the fate of the eye is decided.

Reese[21] is of the opinion that leiomyoma of the iris is radioresistant and that irradiation of any kind is of no avail.

SUMMARY

A case of a leiomyoma of the iris is presented, with a review of the individual case reports found in the literature. The historical and clinical characteristics of the 20 cases are summarized, along with a discussion of the pathology, embryology, diagnosis, and treatment of this rare iris neoplasm.

CONCLUSIONS

1. Leiomyoma of the iris presents a clinical picture of an elevated, nodular, lightly colored, well-circumscribed tumor exhibiting vascularity, usually being confined to the lower iris quadrants without involvement of the angle, and with the pupillary reactions remaining normal. This tumor usually occurs in middle-aged persons of the Caucasian race, is asymptomatic, and is usually of long

duration. The vision and intraocular tension are usually normal.

2. Leiomyoma of the iris may present a very characteristic clinical picture, but its rarity and close resemblance to lightly pigmented melanoma make the clinical diagnosis difficult.

3. Negative radioactive phosphorus (P^{32}) uptake studies may help to differentiate this benign neoplasm from malignant melanoma, but further studies are required to establish this diagnostic test.

4. Diagnosis of leiomyoma of the iris rests on specific pathologic criteria, including special stains for myoglia fibrils, which should be fully explored in all possible cases.

5. Total excision of leiomyoma of the iris, or other well-localized iris neoplasms, by iridectomy is recommended as the treatment of choice whenever total removal of the tumor is possible because of localized iris involvement and the absence of angle involvement.

REFERENCES

1. Berliner, M. L.: Biomicroscopy of the Eye, Vol. II, New York, Paul B. Hoeber, Inc., 1949.

2. Blodi, F. C.: Leiomyoma of the Ciliary Body, Am. J. Ophth. **33**:939, 1950.

3. Bossalino, G.: Di una non comune osservazione de leiomyoma maligno del corpo ciliar e dell'iride, Boll. ocul. **13**:332, 1934.

4. Davis, W. T.; Sheppard, E., and Romejko, W. J.: Leiomyoma of the Iris, Am. J. Ophth. **27**: 467, 1944.

5. Duke-Elder, W. S.: Text-Book of Ophthalmology, Vol. III, St. Louis, C. V. Mosby Company, 1945.

6. Duke-Elder, W. S., and Stallard, H. B.: Leukosarcoma of the Iris, Brit. J. Ophth. **14**:158, 1930.

7. Eisenberg, I. J.; Terner, I. S., and Leopold, I. H.: Use of P^{32} as an Aid in Diagnosis of Intraocular Neoplasms, A. M. A. Arch. Ophth. **52**:741, 1954.

8. Ellett, E. C.: (A) Leiomyoma and (B) Hematoma of the Iris, Arch. Ophth. **21**:497, 1939.

9. Ferrer y Paisan, O.: Tumores del iris; los leiomiomas, Arch. Soc. estud. clin. Habana **42**:105, 1949.

10. Fleming, N.: A Case of Pigmented Leiomyoma of the Iris, Brit. J. Ophth. **32**:885, 1938.

11. Friedenwald, J. S., and others: Ophthalmic Pathology: An Atlas and Textbook, Philadelphia, W. B. Saunders Company, 1952.

12. Frost, A. D.: Leiomyoma of the Iris, Am. J. Ophth. **20**:347, 1937.

13. Fulgosi, A.: Ein Fall von Leiomyom der Iris, Ophthalmologica **125**:155, 1953.

14. Heath, P.: Tumors of the Iris Muscles, Tr. Am. Ophth. Soc. **49**:147, 1951.

15. Kahler, J. E.; Wallace, W. E.; Irvine, R., and Irvine, A. R.: Leiomyoma of the Iris, Arch. Ophth. **29**:479, 1943.

16. Kirby, D. B.: A Technique for Total Biopsy of Neoplasms of the Iris: Report of a Case of Excision of Leiomyoma, Am. J. Ophth. **36**:1225, 1953.

17. Li, T. M.: Primary Ring Sarcoma of the Iris, Am. J. Ophth. **6**:545, 1923.

18. Mann, I.: Development of the Human Eye, New York, Grune & Stratton, Inc., 1950.

19. Moulton, E. C., and Moulton, E. C., Jr.: Leiomyoma of the Iris, Am. J. Ophth. **31**:214, 1948.

20. O'Day, K.: Leiomyoma of the Iris, Brit. J. Ophth. **33**:283, 1949.

21. Reese, A. B.: Tumors of the Eye, New York, Paul B. Hoeber, Inc., 1951.

22. Reese, A. B.: Pigmented Tumors, Am. J. Ophth. **30**:537, 1947.

23. Sanders, T. E.: Intraocular Biopsy: An Evaluation, Am. J. Ophth. **36**:1204, 1953.

24. Stanworth, A.: A Case of Leiomyoma of the Iris, Brit. J. Ophth. **34**:633, 1950.

25. Thompson, A. H.: Tumor of the Iris, Tr. Ophth. Soc. U. Kingdom **19**:49, 1899.

26. van Duyse: Leiomyome sarcometode, leiomyome malin de l'iris, Arch. opht. **31**:13, 1911.

27. van Heuven, G. J.: Leiomyoblastoma Iridis, Ophthalmologica **103**:308, 1942.

28. Verhoeff, F. H.: A Case of Mesoblastic Leiomyoma of the Iris, Arch. Ophth. **52**:132, 1923.

29. Wood, C. A., and Pusey, B.: Primary Sarcoma of the Iris, Arch. Ophth. **31**:323, 1902.

30. Zentmayer, W.: Primary Sarcoma of the Iris; Removed by Iridectomy; No Recurrence in 3½ Years, Tr. Am. Ophth. Soc. **28**:109, 1930.

A Technique for Goniophotography

SEYMOUR GOODSTEIN, M.D.
A. A. CINOTTI, M.D.
MORTIMER CHOLST, M.D.
and
JOHN P. GOELLER, New York

Since practically everybody considers himself a photographer of sorts, we became intrigued with the possibility of photographing our gonioscopic findings. A simple, effective method of goniophotography would provide the two great advantages of all photography, i. e., a permanent record of the situation at the moment and an ideal source of teaching material.

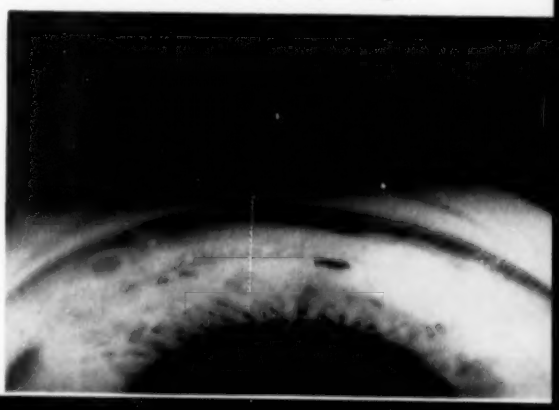
Our first efforts were directed toward the use of the slit lamp as a source of illumination. This proved extremely difficult, and we realized that a small illuminator which would be hand-held would be advantageous. Such an instrument was constructed. The original, which we are still using, was made from a Band-Aid can. An aperture was cut at one side to direct the light. Two sockets were placed at the bottom. A standard automobile taillight bulb was placed in the back socket. In front of this a flash bulb was inserted. A strip of Lucite was placed between the flash bulb and the aperture to protect the patient. The can was lined with aluminum foil to serve as a reflector. The entire unit was connected to a battery box, which served as a power source.

The camera used was a flash-synchronized, single-lens reflex type, with a prism reflex viewer added to make focusing easier. Extension tubes were added to give additional magnification. A bellows attachment on a micrometer carriage was placed between the lens and the tubes to facilitate fine adjustment, since the focusing is quite critical. The magnification achieved was about three times.

We have used both the Allen Gonioprism, and the Goldman lens, with one and three

Fig. 1.—Normal open angle.

Fig. 2.—Foreign bodies (glass) in angle.



This study was aided by a grant from the Alfred P. Sloan Foundation.

From the Department of Research, New York Eye and Ear Infirmary, and the service of Dr. J. Gordon Cole.

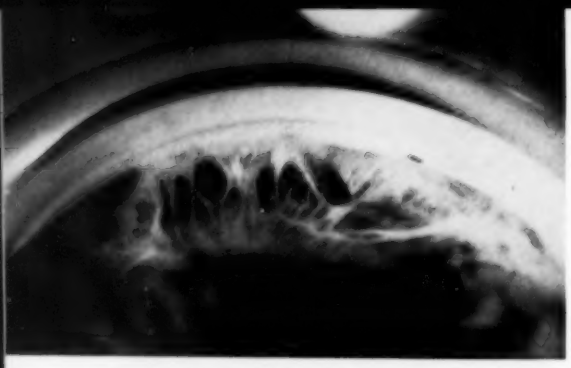


Fig. 3.—Broad anterior peripheral synechiae.

prism faces. Their relative efficiency seems to depend on the familiarity of the observer with the particular instrument. In all cases we made an attempt to see the entire angle.

The technique used is as follows: The patient is seated at the table, and preliminary adjustments are made of the forehead and chin rests. After instillation of tetracaine (Pontocaine) hydrochloride 0.5%, methylcellulose is placed in the goniolens cup, and the lens is inserted. With an assistant holding the light source and directing it into the lens, the angle is visualized. This is done with the camera diaphragm wide open. The operator holds the lens in one hand, manipulating it to bring the area into view. After the area to be photographed is brought into proper focus, the assistant closes the camera diaphragm and the operator trips the shutter, setting off the synchronized flash bulb. The bulb may then be changed by the assistant if additional views of the same or other parts of the angle are to be photographed. An SM bulb is used at an aperture of 5.6.

With the apparatus and technique we have described, we are able to photograph the anterior chamber angle quite easily. The magnification achieved is sufficient to demonstrate details accurately. Apart from its use in glaucoma, a permanent record of conditions such as foreign bodies or pigmented masses in the angle may be recorded and followed in serial studies. This affords the ophthalmologist an opportunity to observe any changes which may take place.

Ocular Effects Produced by High-Intensity X-Radiation

PAUL A. CIBIS, M.D., St. Louis
WERNER K. NOELL, M.D., Buffalo
and
BERTRAM EICHEL, D.D.S., Randolph Field, Texas

One of the outstanding features of radiation damage is the difference between embryonic and adult tissues and their reactions and the manner in which these reactions are manifested (Hicks *; Russell [4]; Wilson and Karr [5]; Wilson, Jordan, and Brent,[6] and Warkany and Schraffenberger [7]). The sequence of x-ray-induced developmental abnormalities and a strict timetable of their genesis have been established in rats and mice by Hicks.[3] He demonstrated a certain resistance of the embryonic tissue toward x-ray doses in the range of 100-200 r during the first eight days of gestation. No measurable damage resulted, and the newborn rat appeared normal. Doses ranging from 300-400 r and administered to the rats during the first eight days either destroyed the embryos or resulted in normal newborn rats. The same doses applied at a later time led to definite developmental defects.

In Anderson's textbook of "Pathology,"[8] the lymphoid tissues, immature cells of bone marrow, germinal cells, and epithelial cells of intestine and stomach are classified as radiosensitive; i. e., they are seriously affected by x-radiation of less than 2500 r. The conjunctiva, cornea, and lens are classified as radioresponsive; i. e., they are seriously damaged if irradiated with doses of from 2500 to 5000 r. Brain and retina are classified as radioresistant; i. e., more than 5000 r is necessary to kill or injure a significant number of cells. Retinal changes following x-irradiation with 1000 r, however, have been observed by Vogel[9] in newborn mice. These changes consisted of cellular disorganization, destruction, and nuclear degeneration, occurring within 24 hours. Necrosis of retinal rod cells in adult rats which had been killed between 6 and 11 days after head irradiation with 1500 to 5000 r has been reported by Hicks and Montgomery.[10] In their recent study, Hicks and Wright † compared the acute effects of several types of ionizing radiations, especially on the nervous system. They observed destructive changes of the retinal rod and ganglion cells produced by cathode rays administered in doses of 20,000 to 30,000 rep within one second, whereas doses of 40,000 rep always killed the animals within a few seconds. In their report concerning the effect of local brain x-irradiation on the pinna reflex, Gerstner, Konecci, and Taylor [11] gave a preliminary account of retinal damage in guinea pig eyes which had been examined by one of us (P. A. C.). These animals were exposed to 8000 r of x-radiation. Edema was ophthalmoscopically noticeable only in those animals characterized by a more or less heavily pigmented fundus. Albinotic retinas showed either no edema or very slight edema visible only ophthalmoscopically.

From the Departments of Ophthalmology, Neuropsychiatry, and Pathology, U. S. A. F. School of Aviation Medicine, Randolph Field, Texas.

* References 1 to 3.

† Hicks, S. P., and Wright, K. A.: Variation of Pathologic Response to Radiation with Time Intensity Factors, read at the International Congress of Clinical Pathologists, Washington, D. C., Sept. 9, 1954.

In order to explore this observation in a diversified manner, experiments were undertaken to correlate clinical and histopathological findings with possible biochemical and electrophysiological phenomena. In a preliminary report, Noell, Eichel, and Cibis[12] stated that the electrophysiological and histological changes observable in the retina of rabbit and monkey after whole-head or single-eye exposure to high doses of x-radiation appear almost identical to those changes obtained after systemic poisoning by iodoacetic acid. The effect of the latter has been thoroughly investigated by Noell.‡ Exposure to 3000 to 6000 r of x-radiation caused marked and selective effects upon the electroretinogram (ERG), which have been observed 10 minutes after exposure. The b-wave was found preferentially eliminated in comparison with a- and c-waves. The function of the pigment epithelium was tested electrophysiologically by means of the azide response, as described by Noell.[14] The optic nerve excitability was measured by electrical stimuli and was found unimpaired. When the ERG appeared affected, death of rod cell population was evident histologically within 4 to 10 hours. There was a close correlation between number of dead rod cells and degree of diminution of the b-wave. Death of the rod cells was followed by autolysis and absorption without any phagocytosis. After 10 to 12 days, the visual cells had completely vanished, while the inner retinal layers were preserved. In monkeys, the cone cells proved to be more resistant than the rod cells. This is in almost complete agreement with the observations previously made by Noell in his iodoacetic acid experiments.[14] A more detailed description of the electrophysiological behavior and of the histological and biochemical changes in the retina following high doses of x-radiation will be given elsewhere.

In this study we are mainly concerned with a general outline of those histological changes which occur within the eye following exposure to high doses of x-radiation.

‡ References 13 and 14.

EXPERIMENTAL MATERIAL AND METHODS

Animals.—Guinea pigs, rabbits, monkeys, and dogs were used.

1. There were 15 guinea pigs—9 albinotic and 6 pigmented— varying in weight from 238 to 536 gm. They were given whole-head irradiations, and the results obtained were compared with those collected from 10 starved control animals, weighing between 362 and 500 gm. The irradiated animals were killed by decapitation 24 hours after radiation.

2. There were 120 rabbits—60 New Zealand white (NZW) and 60 chinchilla gray—which were divided into three groups of 40 each. Each group of 40 contained 20 New Zealand whites and 20 chinchilla grays. All were virgin does, varying in weight from 2.2 to 3.4 kg. All had been maintained on a stock Purina chow and water diet ad libitum for at least one week prior to the experiments. The 40 animals of Group 1 received total-head x-radiation for 21 minutes and were killed 24 hours after exposure. Food and water were withheld because animals exposed to high-intensity x-radiation restrict their food and water intake during the first 24 hours. The animals of Group 2 were starved for 24 hours and then killed without irradiation. The animals of Group 3 were not irradiated and were fed ad libitum and killed at random. The observations made upon this group of animals were interpreted as normal data and established the state of tissues in each strain just prior to irradiation. Group 3 served as control for Group 2, and comparison established the effect of 24 hours' starvation upon the tissues. The eyes of the irradiated group were examined clinically every hour throughout the 24-hour postirradiation period, and the control eyes of Groups 2 and 3 were similarly examined for 24 hours before the animals were killed. At the end of the 24-hour period, the left eye was removed from each animal and fixed in formalin at 85 C and prepared for histological work-up. The right eye of each animal was enucleated, and homogenates of retina, choroid, and lens were prepared separately for biochemical evaluation.

For the purpose of investigating the electrophysiological and histological aspects of the variations of response which occur with dose and time elapsed after irradiation, another group of 40 NZW rabbits, varying in weight between 2.2 and 3.7 kg., was divided into eight subgroups, which received single-eye or whole-head x-irradiation of various doses, as indicated below. The eyes were examined electrophysiologically 10 minutes after irradiation. Periodic electrophysiological examination followed at certain intervals for as long as 21 days. The animals were killed at various time intervals, and the eyes placed in Zenker's fixative immediately after removal.

3. Two rhesus monkeys received single-eye x-radiation with larger doses.

4. Two dogs were treated with high doses of x-radiation to the whole head. These animals were made available after they had been studied by Chinn,§ whose primary interest centered about the vomiting reflex.

Groups 3 and 4 were included in this report, first, to demonstrate that the radiation effect reported herein is not confined to rodents, and, secondly, to differentiate between rod and cone susceptibility to ionizing radiation.

Irradiation.—Prior to irradiation the guinea pigs were immobilized by a canvas harness—the rabbits and dogs by tying with gauze, and the monkey by Dial or thiopental (Pentothal) sodium anesthesia. A Picker deep therapy x-ray unit was used as the source. In the experiments with guinea pigs, the radiation was administered at a voltage of 260 kv. and at an amperage of 18 ma. The inherent filtration of the x-ray tube was equivalent to 0.25 mm. of copper. A 6 mm. wooden board was interposed between the source and the main part of the brain, while a 30 mm. wooden board was placed between the source and the medullary area, as outlined by Gerstner, Konecci, and Taylor.[11]

For rabbit whole-head irradiation, the tube was closed by a lead shield having a central opening adjusted to the head size of the animal, whereas for single-eye irradiation the central opening of the lead shield was limited to a bore hole of 20 mm. diameter.

The average dose rate administered to rabbits, measured in air at 27 cm. target-eye distance, was about 630 r/min., whereas the average value obtained in the vitreous body of the right and left eyes measured about 275 r/min. The total dose of radiation applied to the rabbits in the biochemical experiments was approximately 5570 r. Dosimetry measurements were made upon a small group of rabbits. These measurements were obtained through the use of a Victoreen Chamber Dosimeter, and will be extended and reported separately elsewhere.‖

The eight groups derived from the 40 NZW rabbits irradiated for the purpose of electrophysiological and histological study received total doses of 1700, 2500, 3300, 4100, 5000, 5500, 6600, and 10,000 r, respectively. The radiation was administered either to the whole head or to the single eye.

The right eyes of the monkeys were irradiated for 25 and 35 minutes, respectively. The left eyes were used as controls. We are well aware of the fact that the left eyes received some stray radiation. Repeated electrophysiological, and later histological, examination, however, proved that the stray radiation did not noticeably affect the control eyes. Dosimeter measurements were not performed. The radiation factors involved in the monkey experiments were as follows: 260 kv.; 18 ma., unfiltered; round field of 20 mm. diameter; source-target distance of 24 cm.; dose rate in air of 1000 r/min., at 21.5 cm. distance. The experimental procedure was, in general, similar to that employed in the rabbit experiments.

The radiation administered to the dogs was given as whole-head exposure, filtered by the insertion of 1 mm. of aluminum sheeting and 0.25 mm. of copper sheeting in the path of the beam. The dose rate for Dog 1 was approximately 69 r/min.; that for Dog 2, approximately 179 r/min. The total dose employed in both cases was about 10,000 r.

RESULTS

The lesions observed clinically in the guinea pigs as result of radiation were predominantly of vascular origin, manifested by moderate or severe conjunctival and ciliary congestion, swelling and narrowing of the pupils, aqueous flare, and retinal edema. The last was visible only in the pigmented retinas, and was usually associated with papilledema. The earliest changes in the retina were visible six hours after exposure. In three cases the edema was mild. In two cases the ophthalmoscopic picture was that of a slight detachment with rippling and corrugation of the milky-appearing retina. Seven of the nine albinotic guinea pigs developed a more or less distinct papilledema. None of these albinotic animals, however, showed any signs of retinal edema.

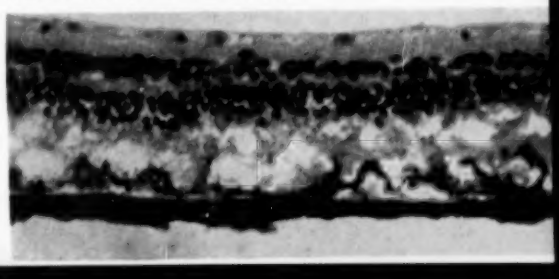
The histological changes ¶ seen in the eyes of the 15 experimental guinea pigs 24 hours

§ Chinn, H. I., U. S. A. F. School of Aviation Medicine, Randolph Field, Texas: Personal communication to the authors.

‖ Lieut. Col. J. E. Pickering and Mr. Everett O. Richey, of the Department of Radiobiology, U. S. A. F. School of Aviation Medicine, directed this aspect of the study.

¶ Technical assistance was given by M/Sgt. John Hughes (histology) and Mr. Ivan Richardson (photography).

Fig. 1.—Retina of guinea pig 24 hours after total-head x-irradiation with 8000 r as measured in air. Pyknosis of rod nuclei, destruction of the external limiting membrane and limbs in bacillary layer, edema of the latter, and of the external nuclear layer. Formalin fixation; hematoxylin-eosin stain; reduced to 76% of mag. × 400.



after irradiation were rather uniform. They represented either conditions of vascular changes of slight or moderate degree or cytological consequences of cellular death, particularly marked in the rod cell population. The features of the former were dilatation of the subconjunctival vessels, swelling of the subconjunctival tissue due to the presence of serous fluid, dilatation of the vessels in iris and ciliary body, and granular precipitation in the aqueous humor. The choroid appeared free of histologically demonstrable pathological changes in the majority of these cases. Only in two cases were granulocytic and mononuclear cell accumulations observed in the choroidal vessels. Hemorrhagic phenomena did not appear in these animals, in contradistinction to similarly treated animals of other species, to be described. The destructive changes which occur within 24 hours in the retinas of irradiated guinea pigs consist mainly of pyknosis of the rod nuclei and more or less complete disintegration of the bacillary layer. In most of the cases the latter appeared distended. The fragmentation of the bacillary layer is taken as evidence of marked friability or brittleness of the limbs of the visual cells due to radiation damage.

The above results obtained from the pilot experiments with guinea pigs are of relatively limited value, since the animals were exposed only to one dose and were killed at a fixed postirradiation time.

In the following series of experiments, utilizing two different strains of rabbits—New Zealand white (NZW) and chinchilla gray (CG)—the radiation was administered to the head or to the single eye. The radiation dose and the postirradiation interval before the electrophysiological and histological examination were both varied in a sufficient number of the albinotic animals to secure both the approximate threshold dose and the minimal dose, given at a fixed rate, which would kill all visual cells. Clinically, the general manifestations of irradiation of the whole head differed greatly from those following single-eye irradiation. After whole-head exposure, the animals' activity lessened and apathy followed. Food and water intake ceased. The rectal temperature of nearly all of a group of 36 such animals exposed to 5750 r increased within two hours from about 37.5 to 39 C and within four hours to from 40 to 43 C. General weakness prostrated all animals with temperatures above 40 C. Some of these animals developed spasm of the hindlegs or of all four limbs, as described by Gerstner, Pickering, and Dugi.[15] Not infrequently, opisthotonos rendered the animals stiff and helpless. Five of the 36 animals died before 24 hours. The remaining animals were killed at 24 hours for histological and biochemical study.

The ophthalmological picture of these whole-head cases was distinguished by signs of blepharoconjunctivitis and iritis, associated with functional, vascular, and cytological changes within the retina, optic nerve, and choroid.

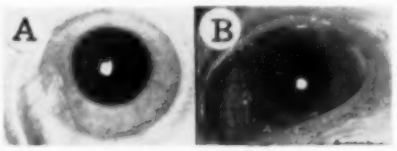


Fig. 2.—(*A*) Normal eye of albinotic rabbit (New Zealand white, NZW); (*B*) appearance of the same eye 24 hours after irradiation to the head (3000 r).

In those rabbits exposed to single-eye radiation, the general clinical effect was of minor consequence. Ophthalmologically, the external effects are fairly well demonstrated by Figure 2. Four to six hours after irradiation the inflammatory response to radiation became visible as irritation, increasing to hyperemia, lid edema, lacrimation, closure of the eye from lid edema, and sometimes a seropurulent exudation. After such lids were cleaned the eye opened (Fig. 2*B*), but to a less extent than is normal. Hyperemia and edema of the conjunctiva due to active congestion gave the eye a bloodshot appearance. Ciliary flush, aqueous flare, and other signs of iritis usually appeared within four to six hours. These signs gradually increased in intensity, reaching their maximum within 10 to 24 hours. At this time the iris showed

loss of luster, blurring, and discoloration, with capillary congestion causing iris rigidity and miosis. The aqueous humor appeared opaque, due to visible floaters and serous exudation. The pupillary light reaction diminished, due partially to increased rigidity of the iris tissue, but largely to the damage of the afferent pathway resulting from the death of the rod cells. This will be detailed elsewhere. The increased permeability of the blood vessels seldom resulted in secondary complications. Increased intraocular pressure and hematogenous infections were observed in only 2 cases out of the 36. In these two cases the cornea was steamy, and the aqueous humor appeared cloudy due to seropurulent exudation. In the remaining cases, however, the course of the postirradiation inflammatory reaction was mild, and the vascular response predominated over the cellular reactions. This was the case when doses higher than 3000 r were applied.

The ophthalmoscopic changes were inconsistent. There was, however, a definite difference in the ophthalmoscopic picture of albinotic eyes as compared with that of the pigmented eyes. The appearance of the albinotic retina did not significantly change even when the intensity of x-radiation exceeded 3000 r, although papilledema and congestion of the retinal vessels sometimes developed after five hours or more. Hemorrhagic phenomena were observed in only 4 cases among the 67 irradiated rabbits of both strains. The hemorrhages were located at the optic disc in three of these cases. In the fourth it was located slightly temporally and inferiorly, as compared with the location of the other three. In all these cases severe iritis and cloudy exudates in the aqueous humor accompanied the hemorrhagic retinal manifestations of radiation damage. They prevented appropriate photography of the fundus.

The pigmented rabbits, on the other hand, showed one of the most puzzling postirradiation phenomena observed in this study. These rabbits developed an orange-peel or pigskin pattern of the retina. Figure 3 represents such a retina as it appeared before, and 24 hours after, irradiation with 6600 r to the head. These changes were interpreted by us as manifestations of subretinal exudation. Histological studies of these cases showed that pigment granules adherent to the slightly detached retina were the cause of the described orange-peel pattern. This phenomenon was not observed clinically in the eyes of albinotic animals, although the total number of NZW rabbits exceeded that of CG rabbits. Histologically, there were no differences found in the retinas of NZW and CG rabbits other than the difference in pigmentation.

The clinical observations of the effects of radiation on the eyes of dogs and monkeys were, in general, similar to those described in rabbits. Since the number of these animals was small and systematic clinical follow-up was not possible, for technical reasons, this portion of the study will be confined to the histological changes which followed exposure to high-intensity x-radiation.

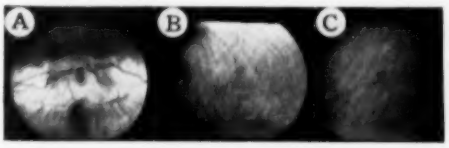


Fig. 3.—Fundus of chinchilla gray (CG) Rabbit: (*A*) optic disc; (*B*) area below optic disc prior to irradiation; (*C*) 24 hours after exposure to radiation (6600 r) measured in the orbit. Note pigskin appearance of retinal surface in irradiated eye.

HISTOPATHOLOGY

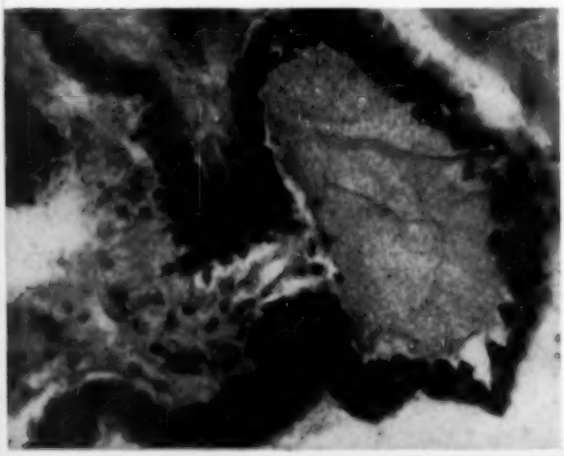
The tissue damage caused by high-intensity x-radiation within the mammalian eye was of two kinds: (1) nonspecific inflammatory reactions, and (2) specific reactions, which resulted in early death of selected neural elements in the retina.

1. The nonspecific inflammatory reaction consisted predominantly of vascular congestion, exudation, interstitial edema, and swelling of the cytoplasm of epithelial and endothelial cells. Serous exudate in the anterior chamber appeared three to four hours following a dose to the eye greater than 2000 r. Granular precipitated proteins appeared in

Fig. 4.—Cornea and anterior chamber of right eye of albinotic rabbit (NZW) 12 days after single-eye x-irradiation with 3300 r. Granular precipitates in anterior chamber and acidophilic membrane of fibrin covering the damaged endothelium. Zenker fixation; hematoxylin and eosin; reduced to 76% of mag. × 600.

the anterior chamber at later stages. Not infrequently these formed an acidophilic membrane lining the corneal endothelium (Fig. 4). Swelling of the vascular layer of the ciliary body and its processes occurred within five hours after irradiation. At later stages a meshwork of acidophilic strands of fibrin appeared within the edematous spaces of the ciliary processes (Fig. 5). In a few cases perivascular and interstitial hemorrhage accompanied the vascular changes described above (Fig. 6).

Fig. 5.—Fibrinous exudate in ciliary process of CG rabbit exposed to 10,000 r. Zenker fixation; hematoxylin and eosin; reduced to 73% of mag. × 1000.



The cytological reactions provoked by the radiation trauma was generally mild and limited to the appearance of mononuclear wandering cells and polymorphonuclear leucocytes, usually enmeshed within the filtration angle.

Endogenous infection occurred in two animals during the second postirradiation week. Histologically, these showed severe fibrinous exudation into the anterior chamber, accompanied by a few polymorphonuclear granulocytes and mononucleocytes. The corneal endothelium vanished (Fig. 7), causing the observed loss of corneal transparency by allowing cornea imbibition of fluid. Inflammatory changes in the iris, ciliary body, and choroid also occurred. These included vascular congestion, hemorrhage, edema, and subsequent atrophy, varying both in severity and in the area involved. Instances of these choroidal changes will be discussed in conjunction with the description of radiation damage of the retina.

2. The specific reactions within the retina following high doses of x-radiation consisted of early death of selected neural elements. These reactions followed a pattern. We found that a single dose of 2000 r caused cessation of function of a great part of the rod cell population. This occurred in adult animals, and within less than 10 minutes. This early effect was evidenced on the ERG by the preferential disappearance or attenuation of the b-wave potential, as compared with c- and a-waves (Noell and associates).

Histological changes, however, became visible only after a latent period of four to six hours. These included signs of cell death, such as pyknosis of the rod cell nuclei, structural disintegration of the bacillary layer, or destruction of the rod cell in toto. These phenomena always followed b-wave attenuation, and their severity correlated well with the degree of b-wave impairment.[12]

Figure 8 represents the normal albinotic rabbit retina at the ora serrata. Figure 9

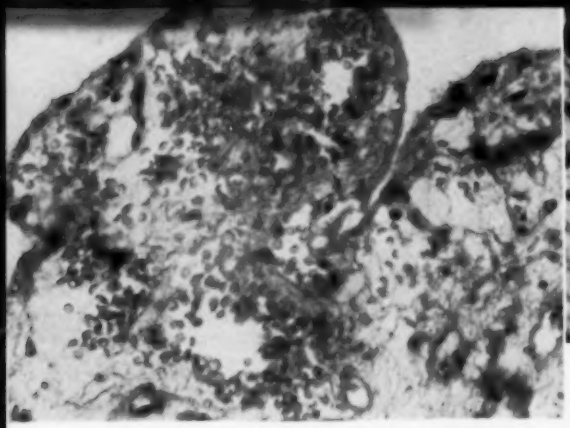


Fig. 6.—Rarification of ciliary epithelium. Hemorrhage and edema of interstitial tissue in vascular layer of ciliary body of albinotic rabbit 12 days after irradiation with 3300 r. Zenker fixation; hematoxylin and eosin; reduced to 75% of mag. × 400.

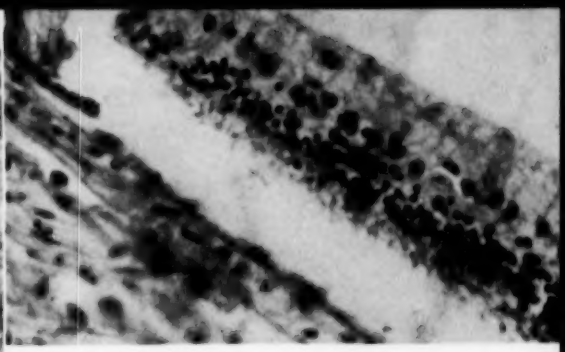


Fig. 9.—Ora serrata of NZW rabbit six hours after x-irradiation to the head; 5500 r administered to the eye. Pyknosis of visual cell nuclei, disintegration of their structural organization, destruction and crumbling of membrana limitans externa and visual cell limbs. Pigment of epithelium slightly damaged. Note beginning of cytoplasmic swelling of cells of the internal nuclear layer. Zenker fixation; hematoxylin and eosin; reduced to 73% of mag. × 400.

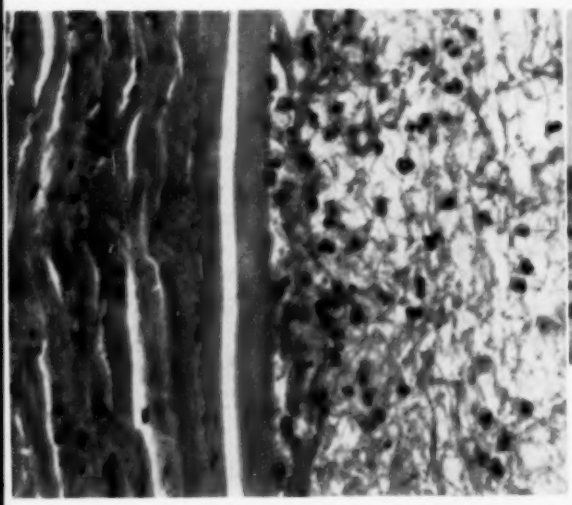


Fig. 7.—Cornea and anterior chamber of NZW rabbit 18 days after x-irradiation with 5000 r to the eye. Fibrin network enmeshing polymorphonuclear leucocytes and mononuclear cells. Note that corneal endothelium has vanished. Zenker fixation; hematoxylin and eosin; reduced to 74% of mag. × 800.

Fig. 8.—Ora serrata of control eye, NZW rabbit. Retina artificially detached and dislocated toward the ciliary body. Zenker fixation; hematoxylin and eosin; reduced to 73% of mag. × 400.

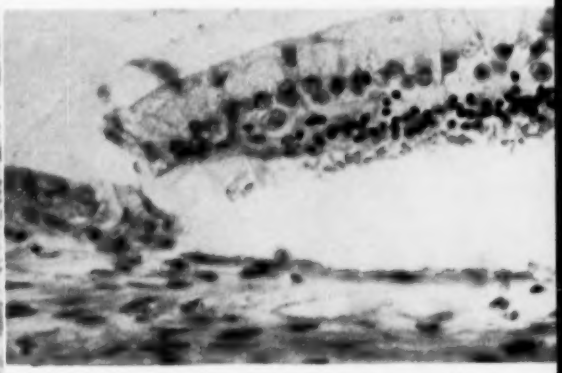


Fig. 10.—Ora serrata 27 hours after irradiation to the head; 5500 r to the eye. Advanced pyknosis and autolysis of pyknotic nuclei, beginning cytoplasmic swelling of cells in external nuclear layer, swelling of cells in internal nuclear layer. Destruction of visual cell limbs and external limiting membrane. Vacuolation of some pigment epithelial cells. Zenker fixation; hematoxylin and eosin; reduced to 73% of mag. × 400.

Fig. 11.—Ora serrata of NZW rabbit 46 hours after x-irradiation to the head; 5500 r to the eye. Advanced pyknosis and autolysis of visual cell nuclei. A few nuclei preserved their chromatin structure. Cytoplasmic swelling of cells of internal nuclear layer. Zenker fixation; hematoxylin and eosin; reduced to 69% of mag. × 400.

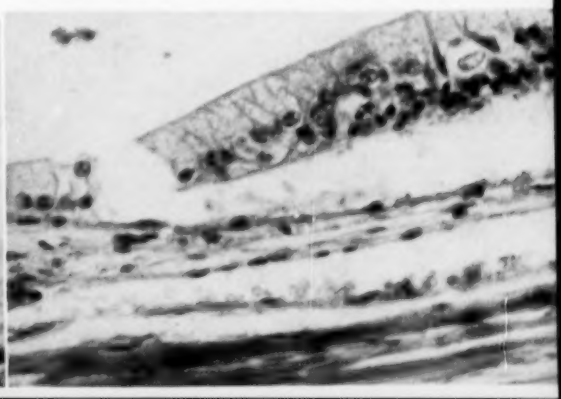


Fig. 12.—Ora serrata of NZW rabbit, 12 days after x-irradiation (6600) r) to the right eye. Almost complete disappearance of visual cells and adjacent layers. Zenker fixation; hematoxylin and eosin; reduced to 73% of mag. × 175.

shows an analogous retinal tissue section six hours after 5500 r eye irradiation. At this stage of postirradiation damage, pyknosis of visual cell nuclei, disintegration of their structural organization, and destruction and crumbling of the external limiting membrane and of the visual cell limbs have fully developed. The pigment epithelium has been little affected. There is early cytoplasmic swelling of the cells in the inner nuclear and ganglion cell layers, which becomes more marked in later stages (Figs. 10 and 11). As the damage continues to develop and the number of nuclei decreases, the space between cells increases. This is indicative of progressive autolysis, a process which apparently occurred in all cases without causing a phagocytic response.

After 12 days nearly all structural components of the neuroepithelium have vanished (Fig. 12). The cytoplasmic swelling has decreased. In this particular section the pigment epithelium appears slightly rarefied. In many other sections the pigment epithelial cells exhibit cytoplasmic swelling and changes in size and shape of the nuclei. In some cases pigment epithelial cells are markedly attenuated in number. In late states, degeneration of the pigment epithelium often accompanied the degenerative changes of the retina.

Retinal damage at the postequatorial region is shown in Figures 13 and 14. Figure 14 shows atrophy and virtually complete disappearance of the choroid, in addition to destruction of the retina. An extensive hemorrhage is visible within the choroidal space.

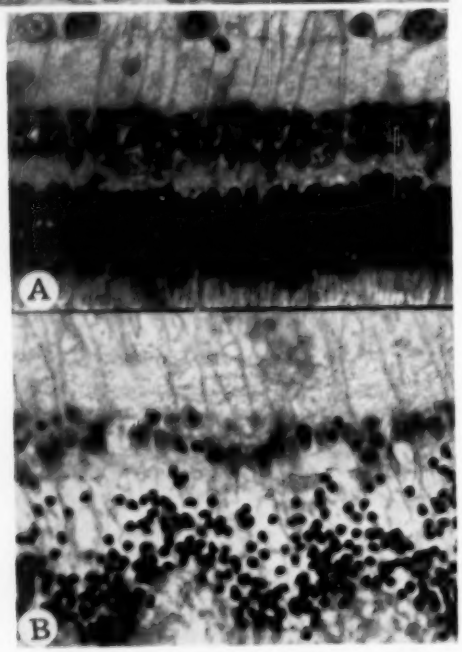


Fig. 13.—Postequatorial portions of rabbit retina (NZW); (*A*) control eye, (*B*) six hours after x-irradiation to the head (5500 r at the right eye). Note pyknosis of visual cell nuclei, edema of external nuclear and plexiform layers, loss of membrana limitans externa, fragmentation and swelling of the limbs in bacillary layer of radiated eye. Zenker fixation; hematoxylin and eosin; reduced to 90% of mag. × 400.

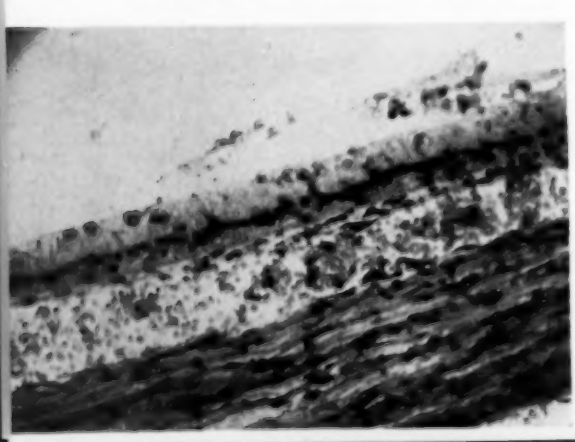


Fig. 14.—Retina of NZW rabbit 12 days after single-eye x-irradiation (5500 r). The outer nuclear layer, external limiting membrane, and bacillary layer have almost vanished. Atrophy of retinal pigment epithelium, Bruch's membrane, and choroid. Diffuse hemorrhage between remainder of retina and sclera. Zenker fixation; hematoxylin and eosin; reduced to 73% of mag. × 175.

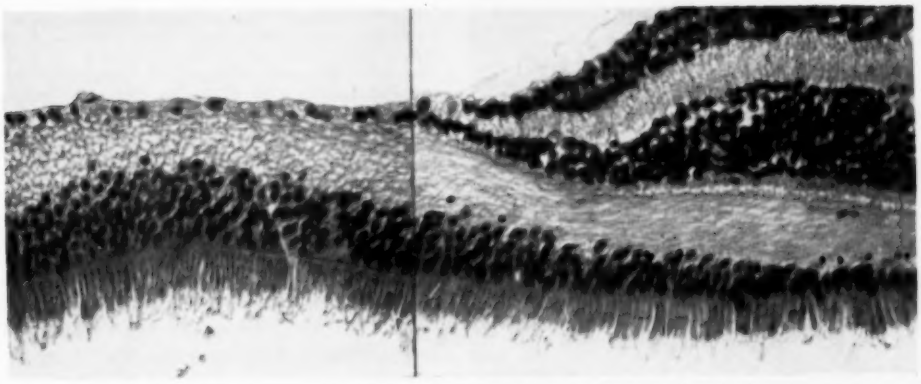


Fig. 15.—Macular-paramacular region of rhesus monkey eye 16 days after single-eye exposure (25,000 r). Macular area appears normal. In paramacular area merely a few pyknotic rod nuclei indicate postirradiation damage. Cone nuclei and limbs normal. Zenker fixation; hematoxylin and eosin; reduced to 65% of mag. × 400.

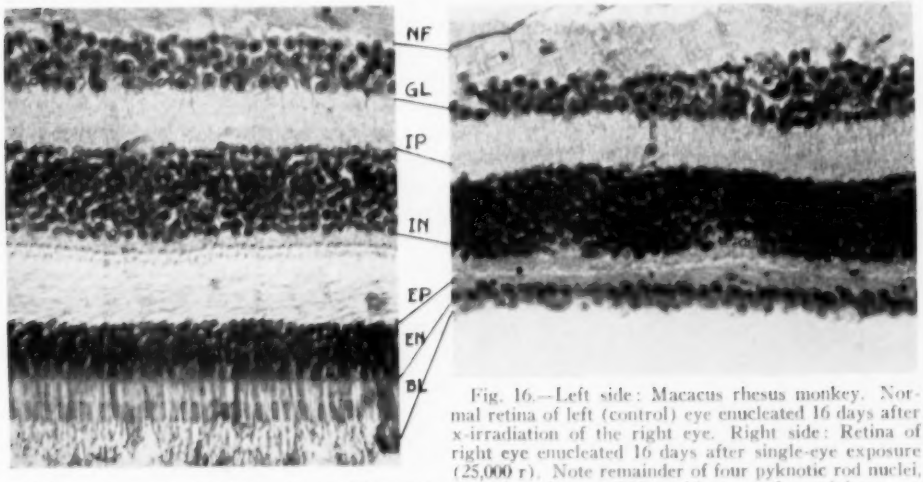


Fig. 16.—Left side: Macacus rhesus monkey. Normal retina of left (control) eye enucleated 16 days after x-irradiation of the right eye. Right side: Retina of right eye enucleated 16 days after single-eye exposure (25,000 r). Note remainder of four pyknotic rod nuclei, shrinkage of external plexiform layer (*EP*), external nuclear layer (*EN*), with row of surviving cone nuclei and stumps of degenerated cone limbs. Limbs of rods have vanished. Zenker fixation; hematoxylin and eosin; reduced to 65% of mag. × 400.

The following section concerns the monkey's retina, which possesses both rods and cones. In normal monkeys the fovea contains only cones; in the parafoveal area of the macula, a few rods are interspersed, the proportion of rods to cones gradually increasing from the paramacular area toward the periphery.

Figure 15 shows the macular area of the irradiated monkey eye 16 days after exposure

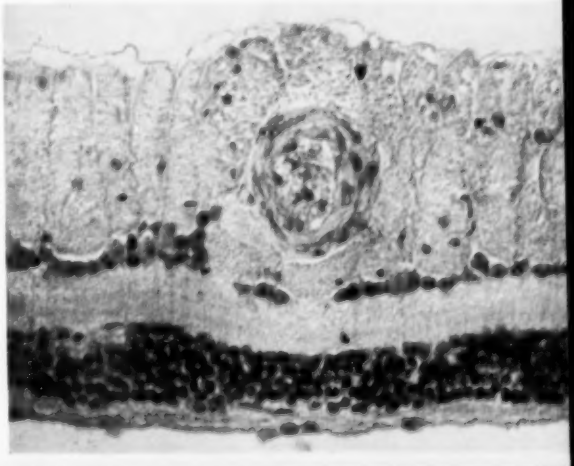


Fig. 17.—Rhesus monkey, cross section through nerve fibers lateral to optic disc, 16 days after single-eye exposure (25,000 r). Note that nearly all visual cells (except five cone nuclei) vanished. Thickened wall of retinal vessel shown. Zenker fixation; hematoxylin and eosin; reduced to 75% of mag. × 400.

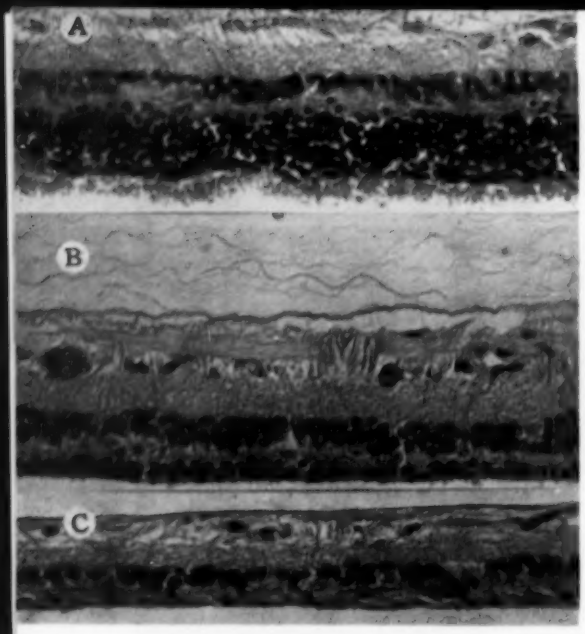


Fig. 18.—Dog retina. *A*, right eye removed 24 hours after total-head x-irradiation (10,000 r). Note pyknosis of visual cell nuclei and edema of nerve fiber layer. *B* and *C*, left eye of same animal removed eight days after irradiation. Note cytoplasmic swelling of ganglion cells, pyknosis of rod nuclei, normal chromatin structure of cone nuclei. Complete disappearance of bacillary layer. Retina in *C* further peripheral than in *B*.

Fig. 19.—Rhesus monkey, retina, seven hours after x-irradiation to single eye (35,000 r). Nuclei of visual cells, bipolar, and ganglion cells exhibit pyknosis, cytoplasmic swelling, and vacuolation. Destruction of membrana limitans externa and bacillary layer evident. Zenker fixation; hematoxylin and eosin; reduced to 76% of mag. × 400.

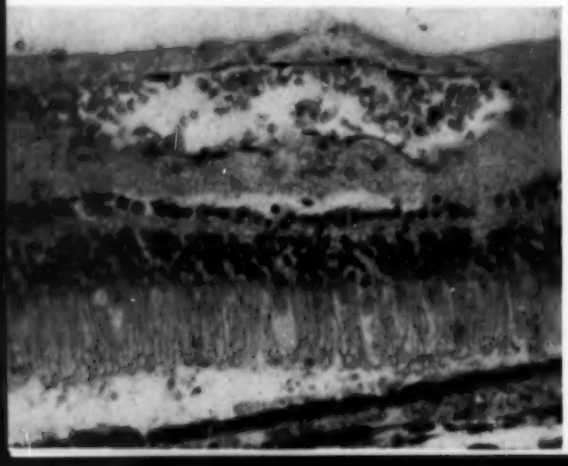


Fig. 20.—Distended and ruptured retinal capillary. Same animal as that in Figure 19. Zenker fixation; hematoxylin and eosin; reduced to 73% of mag. × 400.

to 25,000 r (total dose as measured in air). In the foveal area the cones appear normal. In the parafoveal area the differences between irradiated and control eyes is confined to the presence of a few pyknotic rod nuclei in the irradiated eyes. The situation changes dramatically as the periphery is approached. Figure 16, left side, represents a normal postequatorial area. The cones and rods show well-preserved limbs (*BL*), nuclei (*EN*), and axons (*EP*). The right side of Figure 16 refers to a similar area, 16 days following irradiation, showing the apparently severely damaged limbs of the cones and rods. Complete destruction, however, is confined to the rods, which have vanished with the exception of the pyknotic remnants of four nuclei. The cone nuclei are preserved, although their members have shrunk down to a small stump at the base of the inner limbs. The neuroepithelial part of the outer plexiform layer has also shrunk to one-sixth its original thickness. Farther in the periphery (Fig. 17) the cone nuclei become sparser and sparser as the rod population increases to exceed that of the cones. The breakdown of the cones, not present centrally, might be explained by the fact that they are normally held in position by the adjacent rods. This is in perfect analogy with Noell's original observation of such changes occurring within the eyes of iodoacetic-acid-poisoned monkeys. The peripheral cone changes of IAA-poisoned monkeys were also secondary to degeneration of the rods. It is believed that such changes fully account for what happens to the cones both in the immediate vicinity of the macula and in the periphery. It must be considered, however, that cone cells might

also be affected directly by high doses of x-radiation as well as by IAA.

The conditions caused by high dosage of x-radiation in dogs were quite similar to those observed in monkeys, as illustrated in Figure 18. The histological sections in this instance were all obtained from the eyes of the same animal. The right eye was enucleated 24 hours, the left eye 8 days, following 16,000 r whole-head irradiation. Figure 18*A* (24 hours postirradiation) displays extensive pyknosis of the rods as an early sign of radiation damage. In Figure 18, *B* and *C* (eight days postirradiation) represent conditions of advanced degeneration and atrophy of the outer layers of the retina due to rod destruction. Typical is the preservation of cone nuclei. These conditions are especially noticeable in the periphery of the retina (Fig. 18*C*).

Doses of x-radiation higher than 30,000 r affected cone cells directly and caused death of cone cells, bipolar cells, and ganglion cells, in addition to rod cells, as demonstrated in Figures 19 and 20. These sections are from the retina of a rhesus monkey seven hours following single-eye exposure to 35,000 r (total dose as measured in air, 21.5 cm. source-to-target distance). It is evident that in this case all types of cells in the retina were affected, as evidenced by pyknosis in all retinal cells. In this same retina, congestion was remarkable and was accompanied by severe retinal hemorrhage.

The retinal pigment epithelium, in general, appeared to be more radioresistant than the rod cells. The azide response tested by Noell [12] provided evidence for the assumption that the changes observed within the retinal cells represent primary damage, not secondary changes due to lesions of the retinal pigment epithelium. A more detailed treatment of the problems involving the retinal pigment epithelium will be given in a subsequent report primarily concerned with electrophysiological phenomena.

No attempt was made in this study to investigate the effect of high doses of ionizing radiation upon the crystalline lens.

COMMENT

The effect of high doses of ionizing radiation upon the mammalian eye proved to be very diversified. Electrophysiological, histopathological, and biochemical changes were studied. The histopathological damage involved all ocular tissues with the exception of the sclera. The electrophysiological manifestations of radiation damage provided convincing evidence that the neural elements in the retina are subject to primary radiation damage. The rod cells were irreversibly and fatally damaged by x-ray doses of 2000 r or more. Secondary damage of the cone cells followed. Primary damage of cone cells, bipolar cells, and ganglion cells was observed in one case irradiated with 35,000 r (total dose measured in air, 21.5 cm. source-to-target distance). The death of rod cells following exposure to 2000 r or more is functionally demonstrable by impairment or disappearance of the b-wave of the ERG. This occurs in less than 10 minutes. At this time no other signs of radiation damage are noticeable. The first conclusive histological indication of death of the rod cell develops within four to six hours after irradiation. This was observed in four species of mammals—rabbits, guinea pigs, monkeys, and dogs. Although the number of monkeys and dogs is not sufficient to warrant conclusions regarding these two species as such, total data from all animals are sufficient to make the above definite conclusions applicable to the mammalian eye in general.

What will eventually happen within a person's eye after single-eye exposure to x-radiation of 2000 r or more? The first symptom which such a person will notice is night blindness. This will appear within 10 minutes and will be irreversible. After a latent period of four to six hours symptoms and signs of congestion, exudation, and hemorrhage within the uveal and retinal tissue will become evident. The clinical picture will be that of a severe serous or serofibrinous uveitis, eventually accompanied by papilledema, retinal edema, serous detachment of the retina, and retinal hemorrhage. In one

of our rabbit cases, however, papilledema was associated with spasm of the retinal vessels. The death of the rod cell population is succeeded by degeneration and atrophy of the external layers of the retina, involving secondarily the cones. The cone members lose the mechanical support which is normally supplied to them by the surrounding rod members, the tragic consequence of which is secondary degeneration of the receptor organs of the cones. Constriction of the visual field is the inevitable result, finally leading to "gun barrel" vision. Only the central part of the visual field, corresponding to the macular area of the retina, will remain. With extremely high doses of ionizing radiation there will be immediate blindness. No threshold dose for irreversible primary death of the cone population has been established yet. It can be assumed that the threshold doses for primary cone death will be somewhere between 10,000 and 30,000 r of x-radiation.

The mechanism of radiation damage leading to the observed phenomena in the eyes of guinea pigs, rabbits, monkeys, and dogs is not known. Aspects of interest resulting from the study which might contribute to the understanding of basic changes in certain mechanisms of the cell metabolism will be discussed in subsequent reports.

SUMMARY

The effect of high-intensity ionizing radiation upon the eye of four species of mammals has been investigated. The animals subjected to radiation exposure were as follows: 9 albinotic and 6 pigmented adult guinea pigs, 60 New Zealand white and 102 chinchilla gray adult rabbits, 2 adult rhesus monkeys, and 2 dogs. Adequate numbers of controls were employed.

The head or single eye of the animals was exposed to x-radiation of 260 kvp and 18 ma. The total doses administered ranged from 1700 up to 35,000 r.

Clinical, electrophysiological, and enzymatic responses to high-intensity x-radiation were studied. This report concerns the clinical and histological manifestations. The electrophysiological and biochemical aspects of this study will be covered in subsequent reports.

The major results of this study may be summarized as follows:

1. The functional and histological patterns developing after high-intensity x-irradiation of the eye are fairly consistent and reproducible.

2. High-intensity x-irradiation causes vascular and/or cytological response in all ocular tissues with the exception of the sclera.

3. The most significant change in the eye of adult mammals following high-intensity irradiation is the death of the rod cell population. This becomes functionally noticeable within 10 minutes by changes in the ERG, loss of the pupillary reflex to light, night blindness in monkeys and dogs, and complete blindness in rabbits and guinea pigs.

4. The latent period for the microscopic appearance of rod cell death is about five to six hours.

5. The minimal lethal dose of x-radiation for rod cells, under the conditions of our experiments, lies between 1700 and 2000 r.

6. The minimal lethal dose of x-radiation for cone cells is probably greater than 10,000 r and less than 30,000 r.

7. The deleterious effect of high-intensity x-radiation upon the rod cell population is followed by secondary degenerative changes affecting the cone cells in the periphery of the retina of monkeys and dogs.

8. The changes mentioned in Paragraph 7, above, must gradually result in extreme constriction of the visual field ("gun barrel vision"); those mentioned in Paragraph 6, above, in immediate blindness of the exposed dog, monkey, or man.

9. Transient impairment of photopic vision and blindness, due to retinal edema, papilledema, and vascular disturbances in the eye and brain, can be expected to develop with a latent period of a few hours following exposure to high-intensity ionizing radiation.

REFERENCES

1. Hicks, S. P.: Developmental Malformation Produced by Radiation: A Timetable of Their Development, Am. J. Roentgenol. **69**:272, 1953.

2. Hicks, S. P.: Mechanism of Radiation Anencephaly, Anophthalmia, and Pituitary Anomalies, A. M. A. Arch. Path. **57**:363, 1954.

3. Hicks, S. P.: Effects of Ionizing Radiation on the Adult and Embryonic System, in Metabolic and Toxic Diseases of the Nervous System, A. Res. Nerv. & Ment. Dis., Proc. (1952) **32**:439, 1953.

4. Russell, L. B.: X-Ray Induced Developmental Abnormalities in the Mouse and Their Use in the Analysis of Embryological Patterns: I. External and Gross Visceral Changes, J. Exper. Zool. **114**: 545, 1950.

5. Wilson, J. G., and Karr, J. W.: Effects of Irradiation on Embryonic Development: I. X-Rays on the 10th Day of Gestation in the Rat, Am. J. Anat. **88**:1, 1951.

6. Wilson, J. G.; Jordan, H. C., and Brent, R. L.: Effects of Irradiation on Embryonic Development: II. X-Rays on the Ninth Day of Gestation in the Rat, Am. J. Anat. **92**:153, 1953.

7. Warkany, J., and Schraffenberger, E.: Congenital Malformations Induced in Rats by Roentgen Rays: Skeletal Changes in the Offspring Following a Single Irradiation of the Mother, Am. J. Roentgenol. **57**:455, 1947.

8. Anderson, W. A. D., Editor: Pathology, St. Louis, C. V. Mosby Company, 1948, p. 183.

9. Vogel, H. H., Jr.: Retinal Damage and Cataract Formation Following X-Irradiation of the Heads of Newborn Mice, Progress Report ANL-4676, Biological and Medical Research Division, 1951, pp. 29-40.

10. Hicks, S. P., and Montgomery, P. O'B.: Effects of Acute Radiation on the Adult Mammalian Central Nervous System, Proc. Soc. Exper. Biol. & Med. **80**:15, 1952.

11. Gerstner, H. B.; Konecci, E. B., and Taylor, W. F.: Biological and Medical Aspects of Ionizing Radiation: Effect of Local Brain X-Irradiation on the Pinna Reflex of Guinea Pigs, U. S. A. F. School of Aviation Medicine, Project 21-3501-0005, Report No. 8, 1953.

12. Noell, W. K.; Eichel, B., and Cibis, P. A.: Visual Cells and Pigment Epithelium After High Intensity X-Irradiation, Fed. Proc. **13**:106, 1954.

13. Noell, W. K.: Effect of Iodoacetate on the Vertebrate Retina, J. Cell. & Comp. Physiol. **37**:283, 1951.

14. Noell, W. K.: Studies on the Electrophysiology and the Metabolism of the Retina, U. S. A. F. School of Aviation Medicine, Project Report No. 21-1201-0004.

15. Gerstner, H. B.; Pickering, J. E., and Dugi, A. J.: Biological and Medical Aspects of Ionizing Radiation: Sequelae Following Application of High Intensity X-Radiation to the Head of Rabbits, U. S. A. F. School of Aviation Medicine, Randolph Field, Texas, Project 21-3501-0005, Report No. 15.

Scleral Changes Induced by Diathermy in Retinal Detachment

KENNETH C. SWAN, M.D.
and
LEONARD CHRISTENSEN, M.D., Portland, Ore.

The major phase of contemporary surgical treatment of retinal detachment is the application of diathermy to produce focal areas of heat injury at selected sites in the eye. The surgeon hopes that the proliferation which occurs in the reparative phase of reaction to the injury will lead to the development of chorioretinal adhesions. The procedure is an exacting one, which too often fails because the inflicted injury is inadequate, misplaced, or excessive. In the last instance anatomical reattachment of the retina may take place but function is impaired or lost as a result of immediate heat injury or its complications and sequelae. To improve techniques, more controllable methods of administering diathermy and a better understanding of the reactions of the various ocular tissues to heat are needed. Many clinical impressions have been reported, but relatively fewer data on these two fundamental aspects of the surgical treatment of retinal detachment have been obtained by controlled experiments. The suitability of the various types of diathermy apparatus for ophthalmic surgery needs further investigation, and improved methods of studying reactions of the ocular tissues of thermal injury must be developed. We have been working on these problems for several years and plan additional studies.

In this first report it is our purpose to review some general principles of applying modern diathermy equipment and then to present a study in which a new and improved histologic method has been used to determine factors which influence the extent and degree of immediate heat injury to the sclera induced by this apparatus. It seemed proper to investigate thermal injury to the sclera as a first step because diathermy must be applied to or through this tissue. Some degree of undesirable heat damage to the sclera, therefore, is inevitable, but the extent and significance of this injury often is not evident during the operations. Many observers have reported the unexpected finding of severe scleral damage, or even necrosis, at reoperation or in the microscopic study of enucleated eyes. Other aspects of the treatment of retinal detachment will be covered in subsequent reports.

By diathermy we refer to heat that is induced in the tissues by their resistence to the passage of an alternating current oscillating at such high frequency that a neuromotor response is not evoked. If the temperature is raised only slightly, as occurs when a relatively weak current diffuses through a large tissue area between two large metal plates, only physiologic changes, such as hyperemia, take place. This is "medical diathermy." "Surgical diathermy" results when the current, and thereby the heat, becomes concentrated near a relatively small electrode. Then morphological changes can be induced.

If the heat is moderately intense and is localized to a surface such as the skin, evaporation of the tissue fluid gradually results in drying and shrinkage of the surface layers. This is electrodesiccation. A more intense and penetrating current literally "cooks" the tissues in their own fluid, with a negligible amount of evaporation. This is electrocoagu-

From the Department of Ophthalmology, the University of Oregon Medical School.

Study conducted under grants from the Argosy Foundation and the Manley Foundation.

Presented before the American Ophthalmological Society, June 16, 1954.

lation. Finally, if the current is highly concentrated, a dissolution of tissues in contact with the electrode occurs, although little heat injury takes place in the surrounding tissues. This is electrocutting.

Three factors determine the intensity of heat and, thereby, the type of tissue change induced. These factors are tissue impedance, strength * of the current, and duration of its flow. Impedance to the passage of an alternating current is analogous to resistance of a conductor to the passage of a direct current, but more factors are involved. Tissues differ in their impedance and, thereby, in their response to diathermy. For example, the sclera is a relatively avascular, collagenous tissue which has a high impedance. It, therefore, has a greater susceptibility to heat injury from diathermy than a highly vascular layer like the choroid. In the choroid, heat also is more apt to be spread by the vascular system. This difference is well illustrated by the clinical observation that hemorrhage or areas of reaction may take place at distant points in the choroid following a focal scleral application of diathermy. Also, there are responses to heat injury which are peculiar to certain tissues. For example, heating may result in a marked shortening of collagenous structures. Heat shrinkage of the sclera has been demonstrated experimentally [1] and frequently is observed clinically.

As the intensity of the current in the tissues is increased, more heat will be induced. This heat accumulates and becomes more intense as the time of current flow is lengthened; however, the tissue effects of a less intense current flowing for a longer period are not the same as those of a more intense current flowing for a shorter period. In the longer period there is opportunity for the spread of heat to adjacent tissue. Also, the tissue in proximity with the electrode dries and thereby develops increased impedance. As a result, the tissue heat may increase suddenly or the direction of current flow may change to follow a path of lower impedance. For these reasons best control of intensity and spread of heat generally is obtained with a current strong enough to induce the desired type of effect instantly.

The intensity and spread of heat in the tissues also can be controlled to a certain extent by varying the number, size, and shape of the metal electrodes. Most commonly two electrodes are in contact with the body in different places and the current flows between them. The intensity of the current is greater close to that electrode which has the smaller area of tissue contact. For example, if one electrode is a large plate and the other is a small needle, the heat induced will be more intense at the needle end; therefore, it is called the "active" electrode. Little heat is generated in the vicinity of the larger electrode unless only one edge or a small part of the plate should happen to come in contact with the patient's tissues. In general, then, the smaller the area of electrode delivering current to the tissues, the more localized and intense will be the heat induced. This is why needles, wire loops, and fine blades are used for electrocutting and larger electrodes without sharp edges are used to induce a wider spread of less intense heat in the tissues.

To obtain a spread of current in all directions around the electrode, some surgeons prefer to use only a single electrode. In this case, the patient's body acts somewhat like a condenser. When two electrodes, such as a needle and a large plate, are used, the current tends to flow from one only in the direction of the other along the lines of least impedance. In fact, if two small electrodes are applied close together, the spread of current, and thereby the induction of heat, largely can be confined to the tissue between them. This "duoterminal" technique apparently has received little use in ophthalmic surgery.

We have reviewed briefly the tissue effects of diathermy. Before discussing the types of apparatus used to generate current, it should be reemphasized that tissue effects depend upon the strength of the current, time of flow, and tissue impedance rather than on the type of current and how it is generated; however, knowledge of the different types of current and generators is of importance in the selection of the apparatus which will give the sur-

* Electromotive force and amount of the current.

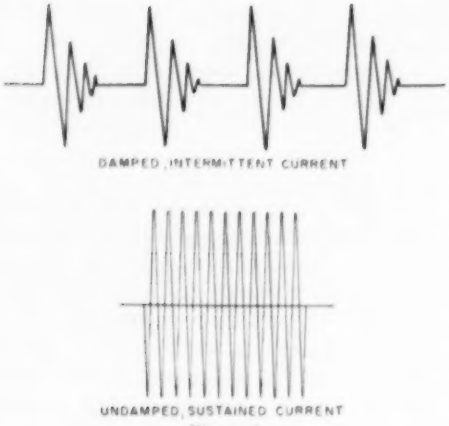


Figure 1

geon best control of the current for a particular procedure.

There are two commonly used methods of generating a high-frequency current. One is by spark-gap generator. This type was developed first and often is spoken of as "conventional" diathermy. The current is said to be "damped" because the amplitude of the oscillating waves varies and the flow of current is not constant. Instead, there are rapidly repeated cycles in which the amplitude rises abruptly and then gradually decreases (Fig. 1). Opportunity occurs for the spread of heat into the tissues around the electrode between the peaks of current. For this reason, an intermittent "damped" current is more suitable for coagulation than for cutting. It is inaccurate, however, to speak of it as a "coagulating" current.

Vacuum-tube oscillators provide a second means of generating a high-frequency current. The current is said to be "undamped" because the amplitude of the waves is unchanging. Also, the flow of current is constant (Fig. 1). As a result intense heat can be localized to focal tissue areas. This type of current is the most suitable for cutting; however, it is being used with increasing frequency for coagulation and fulguration.

There is another important distinction between spark-gap- and vacuum-tube-generated currents. The frequency of spark-gap-generated currents commonly is in the range of 500,000 to 1,500,000 cycles per second (cps), whereas the frequency of vacuum-tube generators may be 10 times as high Some vacuum-tube oscillators generate an "ultra-high" frequency, or "short-wave" current. The higher-frequency currents are receiving increasing favor because the heat induced in tissues of varied impedance is relatively homogeneous. This gives the surgeon better control over both the intensity and the spread of heat in a multilayered structure like the skin or the coats of the eye. The lower-frequency, spark-gap-generated currents are more apt to follow the path of least impedance; therefore, if the surface of a relatively poor conductor, such as the avascular sclera, is dampened with serum or subretinal fluid, the current may be dissipated; conversely, dryness of the tissues may lead to more intense heating than the surgeon has desired. Also, with the lower-frequency currents a contact of the electrode with the tissue must be more exacting; otherwise, sparking occurs. The characteristics of spark-gap- and vacuum-tube-generated currents are summarized in the Table.

In brief, the major tissue effects of surgical diathermy vary from simple dehydration to actual dissolution of the tissues, depending on the intensity of the heat induced. The heat in the tissues increases with the strength of current, the duration of its passage, and the impedance of the involved structure. The current, and thereby the heat induced, becomes more intense and more localized as the active surface of the electrode is decreased in size. More intense and localized heating can be obtained with a constant "undamped" current of relatively high frequency generated by a vacuum-tube oscillator than with the intermittent "damped" current of lower frequency generated by a spark-gap generator. Also, the tissue effects of the higher-fre-

Characteristics of Spark-Gap- and Vacuum-Tube-Generated Currents

Spark-gap-generated current
1. Intermittent
2. Damped
3. Relatively low frequency
4. Relatively long wave length
Vacuum-tube-generated current
1. Constant
2. Undamped
3. Relatively high or ultrahigh frequency
4. Relatively short wave length

quency current are more constant because the flow of current is influenced less by inherent differences in impedance of the various tissues and variations induced by poor electrode contact, dehydration, or the presence or absence of fluid. These general principles have guided us in the selection of apparatus and techniques of application to be investigated in connection with the surgery of retinal detachment.

PRESENT STUDY OF SURGERY OF RETINAL DETACHMENT

In the following experiments, a Model C-350 American Cystoscope Company Electrosurgical Unit was used. It has a spark-gap generator which generates a damped, intermittent current of 500,000 cps and a vacuum-tube oscillator which generates an undamped, constant current of 4,800,000 cps. This first investigation concerned only the factors which determined the nature and extent of immediate heat injury induced in the sclera. Clinical observations correlated with histologic study seemed the best approach; however, we found that the commonly used methods of preparing the eye for histologic study did not satisfactorily demarcate heat-altered from normal sclera. Fortunately, Ross and Walker [2] have described a method of demonstrating alterations induced in collagenous tissues by temperatures as low as 70 to 80 C. We were able to adapt this technique to preparation of the eye for histologic study and to utilize it in this investigation. Details of the technique will be published elsewhere.[3] With it, the normal sclera stains a bright blue, whereas the heat-altered sclera stains an intense yellow-orange.

To standardize techniques and calibrate equipment, preliminary studies were made on animal eyes, but it seemed imperative to conduct experimental work on the human eye. For this purpose we used 12 human eyes which were to be enucleated for other purposes. The sclera was exposed in the course of each enucleation operation so that diathermy could be applied on viable tissues under conditions simulating retinal detachment surgery. The desired types of diathermy current and electrodes were applied. Outward effects, such as shrinkage, were noted, and ophthalmoscopy was performed when there was clarity of the media. The globes were then enucleated for histologic study.

Fig. 2.—Perforating diathermy made with a damped spark-gap-generated current (left) and an undamped vacuum-tube-generated current of higher frequency (right). The zone of lightly stained, heat-damaged sclera around the needle perforation is much larger with the spark-gap-generated current.

In our experimental surgery, an effort was made to duplicate procedures which commonly are used in the surgery for retinal detachment. First, needle electrodes of the type used in "perforating diathermy" were applied with vacuum-tube- and spark-gap-generated currents, alone or blended. Minimal damage was found when strengths of current were used which just would permit ready passage of the needle through the sclera into the choroid. With the higher-

frequency undamped current, the needle could be passed readily into the choroid with considerably less coagulation of the surrounding sclera than with the spark-gap-generated current (Fig. 2). Also, the effects varied much less with the wetness or dryness of the field and with variations in the time of application of electrodes. With the spark-gap-generated current the presence of a little serum or vitreous in the field dissipated the heat and made puncture difficult, whereas if the sclera was permitted to dry, charring was appreciably greater. When the two currents were blended, the extent of scleral coagulation around the perforation was greater than with the higher-frequency current used alone.

fine needle was used with an undamped current of relatively high amperage (Fig. 3). Best control could be obtained when the needle was held 0.5 mm. or less from the sclera, but not in direct contact with it. The current was set at an intensity which would cut away the layers of the sclera without charring. With the spark-gap-generated current we were unable to obtain lesions of this type without considerable charring or desiccation of the surrounding sclera.

In the surgical repair of retinal detachment some surgeons prefer to apply diathermy only to the surface of the sclera. For this technique to be effective, the heat injury must reach the choroid; therefore, we studied

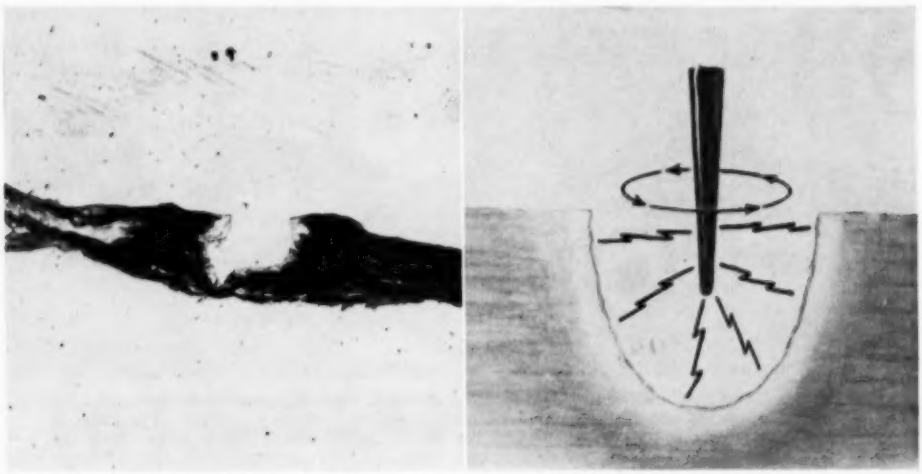


Fig. 3.—Scleral defect with negligible coagulation. A firm needle was held close to but not in direct contact with the sclera. An undamped current of moderate intensity was required.

In the surgical treatment of retinal detachment it sometimes is desirable to make a defect 1 to 2 mm. wide in the outer layers of the sclera so that diathermy can be applied directly to the deeper layers and choroid, or so that an opening through the choroid can be made under direct vision to release subretinal fluid with a minimal risk of accidental injury to the retina. To make the scleral openings, scratch incisions or trephinations are commonly used. We found that an electrocutting technique was simpler, more precise, and less traumatic. A 1 to 2 mm. circular defect could be made with very little coagulation of the surrounding sclera if a very

various methods of inducing a focal area of coagulation extending through all layers of the sclera. Strength and time of application of the current, type of current, and size of the electrode were found to be the important factors.

Currents which were too weak to induce immediate coagulation would shrink and desiccate the surface layers before the heat could build up to coagulating intensity. The treated area would become gray or dirty-white as it became dry and coagulated. We considered this appearance as clinical evidence of an undesirable change because histologic evidence of widespread scleral damage always was

found. A sharply outlined area of increased transparency of the sclera developing almost instantly and confined to the immediate area of application of the electrode seemed the best clinical evidence that heat of coagulation intensity was penetrating the sclera with a minimal amount of undesirable lateral spread. Satisfactory focal coagulation of this desired type could be produced, more consistently with the higher-frequency vacuum-tube-generated current, particularly when hydration of the field was variable. Charring, shrinking, and lateral spread of heat damage in the sclera always were greater with the spark-gap-generated current. Typical samples of lesions produced with the two types of current are illustrated in Figure 4. A 0.5 mm. blunt-tipped electrode was applied to the sclera with just enough current to induce immediate coagulation. Using an electrode with a larger surface area invariably increased the lateral spread of heat injury, although suitable lesions of the desired type could be produced with electrodes up to 2 mm. wide. On the other hand, electrodes with a needle-like point 0.2 mm. or less in diameter were unsuitable for penetrating coagulation unless Pischel's [4] technique of partially penetrating the sclera was used. We confirmed his observation that with the use of a small needle electrode penetrating partially the sclera, coagulation could be obtained extending to the choroid, with minimal lateral spread of heat damage in the sclera; however, it was not always possible to be certain that adequate depth of coagulation was being obtained because the changes at the tip of the electrode could not be observed.

During the surgery for retinal detachment shrinkage of the sclera may result from diathermy. A discussion of the favorable and unfavorable consequences of this occurrence is beyond the scope of the present report; however, it did seem important to establish the determining factors so that shrinkage can be avoided or obtained in accordance with the surgeon's wish. Ocular tension was found to be important. It was necessary to lower the ocular tension by withdrawal of aqueous before gross shrinkage of the sclera could be induced. To create a widespread contraction with a minimal amount of focal damage, a large electrode, such as a 5-mm. metal ball, was more effective than needles or small blunt-tipped electrodes. With a soft

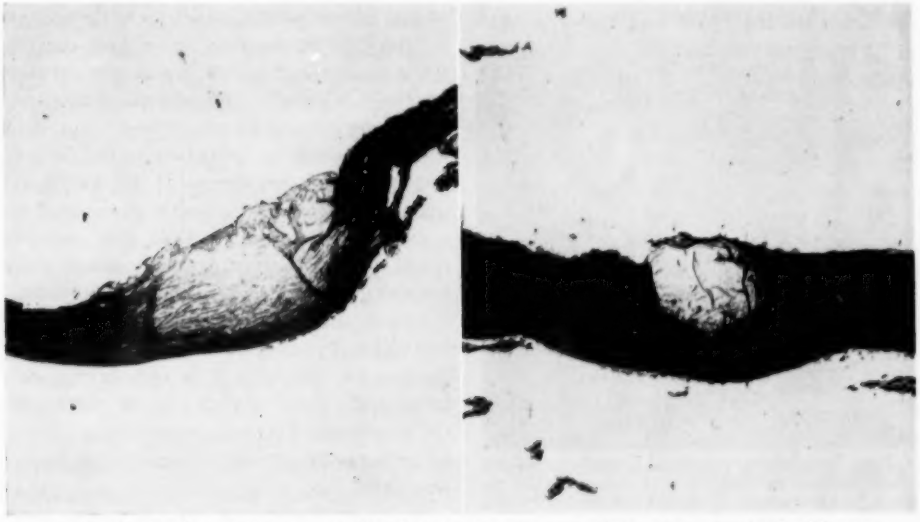


Fig. 4.—Surface diathermy extending into the deeper layers of the sclera. One-half millimeter electrode. Lateral spread of heat damage in the sclera was greater with the damped spark-gap-generated current (left) than with the vacuum-tube-generated current (right).

eye, a low-amperage current applied for only one or two seconds would induce extensive shrinkage before the heat became too intense at the point of contact of the ball electrode. When lower intensities of current were applied for longer periods, gross shrinkage was accompanied by extensive heat damage at the point of electrode contact. More focal damage also resulted with the spark-gap-generated current, probably because a relatively long period of application was required to induce an appreciable amount of shrinkage.

The marked amount of shrinkage of the sclera which can be induced with diathermy is illustrated in Figure 5. In this instance a weak spark-gap-generated current was used.

Fig. 5.—Marked equatorial shrinkage of the sclera induced by diathermy. Ocular tension reduced by paracentesis to permit scleral contraction to occur. The area of contact of the electrode is white, due to desiccation and coagulation. Spark-gap-generated current; ball electrode.

Considerable desiccation and coagulation of the sclera is visible as an ill-defined gray-white area at the point of contact of the electrode. Microscopically, contraction of the surface layers of the sclera was found around this area, whereas the deeper, and apparently unaffected, layers were thrown into folds.

SUMMARY

Diathermy was applied to the sclera of viable human eyes during the course of enucleation operations. General principles of applying surgical diathermy were reviewed and apparatus was chosen accordingly; however, techniques selected were those which commonly are used in the surgical treatment of retinal detachment. Factors determining the degree and spread of immediate heat injury in the sclera were studied by direct observation and by utilizing a new and improved histologic technique of demonstrating heat injury to collagenous tissues; thereby, clinical signs of the various types of thermal injury to the sclera could be established.

Focal areas of penetrating coagulation or dissolution with minimal heat injury to the surrounding sclera best could be obtained by using small electrodes and a strength of current adequate to induce the desired effect almost instantly. To induce a diffuse shrinkage of the sclera with minimal focal damage, a relatively large electrode and a weak current were most suitable, but the ocular tension had to be lowered by withdrawal of aqueous.

The degree and spread of heat induced in the sclera could be better controlled with a relatively high-frequency (5,000,000 cps), undamped, constant current generated by a vacuum-tube oscillator than with conventional (500,000 cps) damped, intermittent current generated by a spark-gap generator; however, additional experiments in which late effects and choroidal retinal and vitreous changes are studied will be necessary to determine the place of each type of current in the treatment of retinal detachment. Also, a wider range of current frequency must be investigated.

Dr. Roger Flanagan, of Coos Bay, Ore., gave many helpful suggestions concerning the use of the apparatus, and Miss Aurelia Allen made the histologic preparations.

REFERENCES

1. Scheie, H., and Bourne, J.: Electrocoagulation of the Sclera: Reduction in Ocular Volume and Pathologic Changes, Am. J. Ophth. **32**:60-78 (June) 1949.

2. Ross, O., and Walker, C.: Histochemical Studies of Thermal Injury on Rat Skin, Proc. Soc. Exper. Biol. & Med. **82**:379-381, 1953.

3. Christensen, L.; Swan, K. C., and Allen, A.: Histologic Demonstration of Heat Injury to the Collagen Tissues of the Eye, A. M. A. Arch. Ophth. **53**:79-81 (Jan.) 1955.

4. Pischel, D. K.: Diathermy Operation for Retinal Detachment: Comparative Results of Different Types of Electrodes, Tr. Am. Ophth. Soc. **42**:543-567, 1944.

Syringoma of the Eyelids

L. EDWARD GAUL, M.D., Evansville, Ind.

The upper and lower eyelids are prominent locations for the tumors of multiple benign cystic epithelioma. During a study of the heredity of this disorder, a patient was seen on whom this diagnosis was made.[1] Characteristic tumors involved the eyelids and were especially noticeable on the lower ones. The patient was not aware of their presence. Palpation caused them to appear more noticeable. Feeling certain that another family of the Princeton Pool * for multiple benign cystic epithelioma had been discovered, I made a search for more subjects. In a large sibship no additional cases were found. A tumor from the midportion of the left lower lid was excised for histological study. The pathological examination revealed multiple benign cystic epithelioma, but, in addition, there were features of syringoma. This finding in itself was not too unusual, but it did suggest correlating more completely the clinical and pathological features of tumors of the eyelids.

Dermal punches were used to remove small growths and nevi; curved scissors and forceps, for papillomas, seborrheic verrucae, and xanthelasma. The small tumors were marked by dotting them with ink. Anesthesia was obtained by inserting the needle away from the tumor and then passing the tip beneath it. Several rotations of the punch freed the tumor sufficiently to allow removal merely by grasping and snipping the subcutaneous tissue. This technique lessened mutilation of the specimens. Usually, the wound required no suturing, owing to the marked elasticity of the tissue. Tumors that might recur had their bases destroyed by electrodesiccation.

Tumors of the eyelids are not common in children; but in middle and late life they adorn more and more lids. The geriatric patients are most prone to them, displaying one or several varieties. Milium, papilloma, and seborrheic verruca are the commonest, with epithelial cyst, intradermic nevus, and epithelioma (benign) next in frequency. Syringoma is commoner than xanthelasma. Less often seen are spider nevus, hemangioma, hidrocystoma, granuloma pyogenicum, and epithelial nevus (dermatosis papulosa nigra). The eyelids and their margins are as amenable to cosmetic surgery as other cutaneous areas. Biopsy specimens are easily and safely obtained. To delay prompt diagnosis of eyelid tumors, especially the small and possible malignant ones, because of the fear of scarring or strictures from biopsies is needless procrastination. Carcinoma of the eyelids and their margins is still seen in much too far advanced a stage.

CLINICAL TYPES OF EYELID SYRINGOMAS

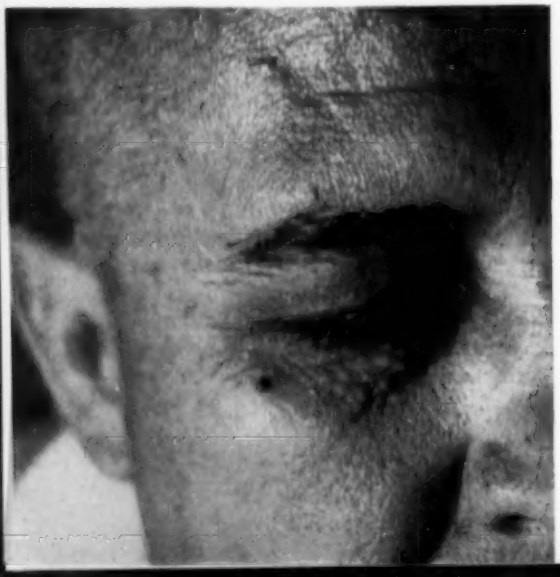
Syringomas can be classed as common benign tumors of the eyelids. Some 30 cases were examined during 1954. The incidence found is mainly a matter of looking for them. Biopsy material was obtained in 14 cases. No inheritance was demonstrated. The lower lid is the favorite site, but only the upper may show them, or both lids may be involved. As a rule, the tumors are bilateral. They have never been seen in children. They make their appearance sometime after puberty. Males and females are about equally affected. No symptoms occur, and most people do not know they have them. No tumors with features of syringoma were seen on the neck,

* Princeton Pool—a term used to designate geographic origin of the Indiana family with multiple benign cystic epithelioma.

Fig. 1.—Case M. S. is a white man aged 38. He was not aware of the small, elongated, yellowish plaques situated over the medial portion of both upper eyelids.

upper torso, or arms of the patient affected. Their growth must be inconsequential, because their size in the late decades of life is about the same as in the middle decades. Histological changes, too, showed no trends in different age groups. Eight patients with xanthelasma did not show any tumors even suggestive of syringoma, nor was xanthelasma seen in patients with syringoma. One patient with clinical and biopsy evidence of lid carcinoma had, in addition, clinical and biopsy evidence of syringoma; but during the same period (1954) five other patients with epithelioma (carcinoma) of the eyelids and eyelid margins showed no clinical evidence of syringoma. It would seem that the anlage of syringoma does not favor lipid infiltration, and that this same anlage is not prone to undergo cellular changes to carcinoma. Three clinical types of syringomas of the eyelids have been found, and these will be described in the order of their incidence.

Fig. 2.—J. B. is a white man aged 41. The duration of the tumors was unknown; he was not aware of their presence. The tumors were distributed bilaterally over the lower lids and the medial portion of the upper lids. They measured 1 to 2 mm. in diameter, were globoid nodules, and presented a pearly-white appearance. Light friction caused them to increase in size.



1. *Plaque Type.*—These tumors have a faint yellowish cast and appear to sit on the surface of the skin. They may be ovoid, elongated, or irregularly rectangular. One plaque was seen almost 0.5 cm. in its long axis. The long axis of the plaque is parallel to the lines of folding of the eyelids (Fig. 1). They are as common on the upper as on the lower lid.

2. *Globoid Type.*—This variety affects both the upper and the lower lid, but is commoner and more pronounced on the lower one. The tumors have a whitish hue, and seem to be embedded in the skin proper (Fig. 2). Their axis, where evident, is also in line with the natural folds of the eyelid. Rarely are these tumors more than 1 or 2 mm. in diameter. One would expect from their color to see more keratinous cysts in the section, but this has not been the case.

3. *Dimple Type.*—Only two cases of this variety have been seen. The distinctive feature is the presence of tumors having a central depression. They look like tiny Lifesavers (Fig. 3), and associated with these are various-sized, globoid masses. The tumors are flesh-colored, and some are as large as 1 cm. in their long diameter.

Greenbaum [9] described the eyelid syringomas as having a slightly yellowish shade which made them stand out from the normal skin (Type 1). He stated that the elevated appearance is lost on stretching the skin but the lesions themselves are not obliterated. On puncture, one obtains only a drop or two of blood. Artom, Cerruti, and Alayon [12] described the tumors as whitish (Type 2) or

yellowish-pink papules (Type 1), ranging in size from that of pinhead to that of a grain of rice. In some cases they noted a superficial resemblance to xanthelasma. Photographs accompany the article.

OBSERVATIONS FROM THE LITERATURE

According to Darier,† there are two types of sweat gland adenomas. 1. Hidradenoma eruptivum. This type is rare. I have seen one case in private practice in the last decade. Discrete, oval, yellowish papules were distributed over the neck and upper torso. They may be found on the face, arms, abdomen, and even the thighs. In the case I saw there were no notes on the record as to whether the eyelids were involved or not. A biopsy specimen from the right anterior chest was reported as typical of syringoma. This section was compared with the sections from the eyelids, and the pathology of the two areas was found to be essentially the same. Andrews [3] shows a photograph of syringocystadenoma of the eyelids, and the impression was gained that the lid tumors accompanied the presence of tumors on the chest, arms, and abdomen. Spinner [4] presented a case of syringoma affecting the eyelids and neck, and at a later date lesions appeared on the abdomen. The pathology accompanied the report. Oliver [5] presented a case of papules distributed over the neck, face, and eyelids. The histological picture was that of syringocystoma. Oliver, in the discussion, mentioned that the section was taken from the eyelid because he and his co-workers thought there would be less scarring if it were removed from this area. Foerster, Foerster, and Wieder [6] presented a patient with tumors affecting the lids and also distributed widely over the torso, arms, and groins. A section removed from the flank was considered to be syringoma. Miller [7] showed a patient with tumors involving the eyelids and the "V" of the neck. Sections from the eyelid and neck were reported as diagnostic of syringocystadenoma. Tavs [8] reported a case with tumors on the neck, axillae, anterior chest, and pubic and crural regions. A section from the pubic region showed syringocystadenoma.

Fig. 3.—M. G. is a white man aged 61. He was unaware of the flesh-colored plaques affecting the upper and lower lids. Some of the tumors were almost 1 cm. in diameter. The elevation above the eyelid surface appeared more pronounced at the periphery. Some of the lesions showed a definite central depression.

2. Hidradenoma of the eyelids. This is the common type and is the subject matter for this report. To my knowledge, only the American dermatological textbook by Greenbaum ‡ describes syringoma of the eyelids as a separate entity. Clinical photographs accompany the description. Anderson,§ in a discussion of a case of syringocystadenoma (syringoma), mentioned that the eyelids and axillae are fairly common sites, and that Pollitzer's translation of Darier's book had a photograph labeled syringoma showing involvement of the lower eyelids. In 1935, Nomland and Scull [11] presented a case of syringocystadenoma affecting the eyelids. When the cysts were ruptured, a watery fluid escaped. Finnerud, in the discussion, considered it to be a hydrocystoma. I have seen four of these cases in the past year, and sections were obtained in all of these. A favorite location is the lid margin, especially the area of the lower punctum of the

† Darier, J., cited by Greenbaum.[2]

‡ Greenbaum, references 2 and 9.

§ Anderson, N. P., in discussion on Novy.[10]

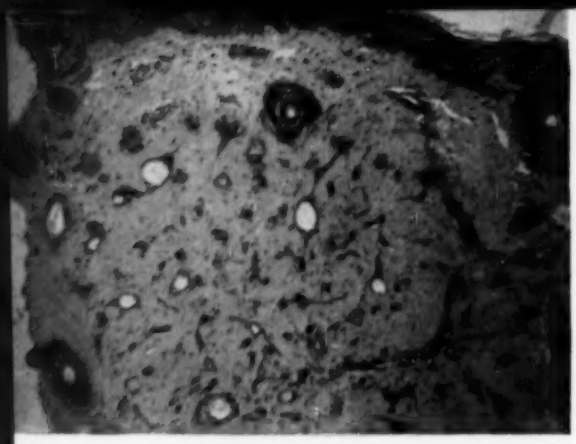


Fig. 4.—Pathology of a tumor from the lower eyelid. Within the cutis are many small cavities lined by irregular epithelium. There are numerous comma-shaped masses of basal cells, some arising from the walls of these cavities. It is difficult to state whether these cavities are taking their origin from sweat ducts or hair follicles. The epidermis shows no significant changes.

nasolacrimal system. Nomland, in the discussion, also considered it to be a hydrocystoma, but mentioned another condition, which he referred to as syringoma, marked by flat lesions having a preference for the eyelids. Nomland, in discussion on the case of Oliver,[5] remarked that the lid tumors were typical of syringoma, and that if one looks for them, one will find them often. During a two-year period, he had seen a dozen of these cases involving only the eyelids, and biopsies in half of them all showed syringoma. The tumors appeared as flat, white papules (Type 2) and were on the lower and upper lids. Finnerud, in his discussion of the case of Oliver,[5] pointed out that he had studied a half-dozen or more biopsy specimens (I assume of the lids), and that histological study differentiates syringoma of the lids from trichoepithelioma. Nomland, in a discussion of the case of Tavs,[8] again stated that there are two types of syringocystoma: the widespread nevoid type, and the type that occurs in women in the 40's and is usually limited to the eyelids. Artom, Cerruti, and Alayon [12] reported six cases, three in females and three in males, of eyelid syringoma.

Summary.—Syringoma may affect only the eyelids, or the eyelids, neck, and torso, or only the neck and torso. The histopathology of a lesion from any area does not seem to differ appreciably (Fig. 4).

PATHOGENESIS OF SYRINGOMA

Sachs ‖ had the opportunity to study 9 biopsy specimens of multiple benign cystic epithelioma, 2 of which were from the eyelids, and 14 syringomas from the eyelids and 1 syringoma from the torso. He interpreted this material as a condition due to changes developing from basal cells. If a basal cell develops into a sweat duct, and the process starts at that point, then a syringoma develops; if it starts within a hair follicle, a multiple benign cystic epithelioma develops, and if the process starts directly from the basal cell margin of the epidermis, one may have a basal-cell epithelioma almost of nevoid type, and one may even have a cylindroma. He places this whole group in a class of adnexal nevoid dermatoses or adnexal nevoid neoplasms. Artom, Cerruti, and Alayon [12] studied the pathological findings in six cases of eyelid syringoma and concluded that syringoma has an epithelial origin; that the epidermic buddings described originate from embryonic sweat gland ducts, and that the elements of syringohidrocystoma originate from apocrine sweat glands and their embryonic buddings. Lever [13] has presented an excellent review of the pathogenesis of benign epithelial tumors and believes that multiple benign cystic epithelioma and syringoma have a common origin in the primary epithelial germ, which has its origin from the embryonal stratum germinativum. Syringomas are basically apocrine gland tumors. Ormsby and Montgomery [14] were unable to see any connection between syringomas and the apocrine glands, but they have seen connections with normal eccrine ducts, but not with mature eccrine glands. The prevalence of syringomas of the eyelids and the ease of obtaining biopsy specimens should help in the elucidation of the pathogenesis of these benign tumors.

SUMMARY

On the basis of distribution and incidence, syringoma may be seen clinically as follows:

‖ Sachs, S. W.: Personal communication to the author.

(1) syringoma of the eyelids; (2) syringoma of the eyelids, neck, and torso, and (3) syringoma of the neck and torso. The histopathology is essentially the same regardless of the site of the biopsy specimens. In some cases of eyelid syringoma, the dermatopathologist finds it difficult not to mention trichoepithelioma. These borderline cases may need a familial history to decide the diagnosis.

509 Hulman Bldg.

REFERENCES

1. Gaul, L. E.: Heredity of Multiple Benign Cystic Epithelioma: "The Indiana Family," A. M. A. Arch. Dermat. & Syph. **68**:517 (Nov.) 1953.

2. Greenbaum, S.: Dermatology in General Practice, Philadelphia, F. A. Davis Company, 1947.

3. Andrews, G. C.: Disease of the Skin, Third Edition, Philadelphia, W. B. Saunders Company, 1946.

4. Spinner, G. J.: Syringoma, Arch. Dermat. & Syph. **33**:381, 1936.

5. Oliver, E. A.: Syringocystoma, Arch. Dermat. & Syph. **33**:390, 1936.

6. Foerster, O. H.; Foerster, H. R., and Wieder, L. M.: Syringocystadenoma, Arch. Dermat. & Syph. **36**:645, 1937.

7. Miller, J. L.: Syringocystadenoma, Arch. Dermat. & Syph. **55**:420, 1947.

8. Tavs, L. E.: Syringocystoma, Arch. Dermat. & Syph. **57**:755, 1948.

9. Greenbaum, S. S.: Syringocystoma of Eyelids, Am. J. Ophth. **11**:275, 1928.

10. Novy, F. G., Jr.: Syringocystadenoma, Arch. Dermat. & Syph. **60**:1043, 1949.

11. Nomland, R., and Scull, R. H.: Syringocystadenoma, Arch. Dermat. & Syph. **31**:148, 1935.

12. Artom, M.; Cerruti, H., and Alayon, F. L.: Sobre a patogenese do siringohidrocistoma, An. brasil. dermat. e sif. **20**:329, 1945.

13. Lever, W. F.: Pathogenesis of Benign Tumors of Cutaneous Appendages and of Basal Cell Epithelioma, Arch. Dermat. & Syph. **57**:679, 1948.

14. Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, Eighth Edition, Philadelphia, Lea & Febiger, 1954.

Physiological Changes in Cornea Induced by Contact Lenses

GEORGE K. SMELSER, Ph.D.
and
D. K. CHEN, B.S., New York

It is well known that conventional contact lenses cause a corneal haze. Recently it has been shown that contact lenses affect the cornea by depriving it of its normal access to oxygen, and that this effect can be abolished if an adequate corneal oxygen supply is made available.* In addition, the effects of contact lenses on the optical properties of the cornea have been duplicated in man by exposing the eye to an oxygen-free atmosphere, thus inducing a relatively anaerobic condition for the cornea. On the basis of these experiments, it was suggested that the cornea maintains its normal water balance by an active metabolic process which requires oxygen, part of which is obtained from air, and that conventional contact lenses, by interfering with the usual corneal access to oxygen, halt the normal dehydrating mechanism. This results in corneal hydration, which causes the observed increase in its thickness and turbidity.

It would be desirable to fortify this argument with some more direct evidence. If the metabolism of the cornea is indeed inhibited by contact lenses because of a limitation in its oxygen supply, one would expect to find an increase in the lactic acid content of the cornea when contact lenses are worn. Such an increase has been observed by Langham [3] in corneas of rabbits when they were maintained in an atmosphere of nitrogen.

A series of experiments was carried out on guinea pigs fitted with contact lenses to determine the effect of such lenses on the amount of lactic acid in the cornea. Measurements were also made of changes in the corneal water content, thickness, and transparency which resulted from contact lens wear.

EXPERIMENTAL STUDY

Guinea pigs (approximately 600 gm.) were found able to wear conventional contact lenses filled with 1.5% sodium bicarbonate solution for many hours without evidence of discomfort, such as inflammation of the conjunctiva. In each case a lens was worn only on the right eye, the left serving as a control. Each animal wore its contact lens for six hours several days prior to the experiment to demonstrate its satisfactory fit.†

(*a*) *Corneal Lactic Acid.*—Contact lenses were worn for periods of one-quarter, one-half, one, two, four, and six hours, at the end of which the guinea pig was killed by a blow on the head and the eyes quickly removed and placed in a small dry beaker packed in ice. The corneas were dissected on an ice-cold, dry glass surface, weighed, and placed in 6% trichloroacetic acid. The concentration of lactic acid was determined by the method of Barker and Summerson.[4] Normal corneas of guinea pigs which had never worn contact lenses were also prepared in this manner to determine the normal variation in the amount of lactic acid in the two corneas. It was found necessary to keep the corneas cold be-

From the Departments of Ophthalmology and Anatomy, Columbia University College of Physicians and Surgeons.

This investigation was supported by the Research and Development Division, Office of the Surgeon General, Department of the Army, under Contract No. DA-49-007-MD-395.

* References 1 and 2.

† The special contact lenses were made in the Obrig Laboratories, Inc., New York, and fitted by Mrs. Margaret Bergman, of that company.

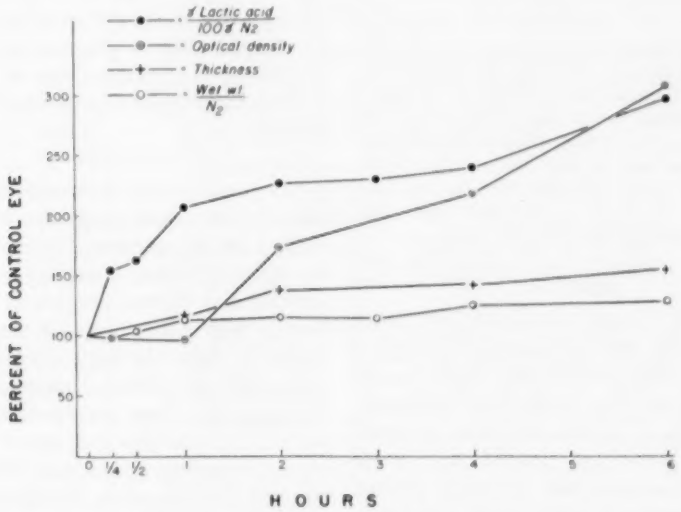
fore placing them in trichloroacetic acid for the time required for their dissection, which, if done at room temperature, would have permitted some change in the lactic acid content, whereas refrigeration decreased its further oxidation.

(*b*) *Corneal Hydration.*—The degree of corneal hydration was indicated by the ratio of the fresh corneal weight to the nitrogen content, the latter being determined by the micro-Kjeldahl method.

(*c*) *Corneal Turbidity.*—It was not found practical to measure turbidity and thickness on the same corneas as those used for the lactic acid determination; therefore, a parallel experiment on other animals was conducted in which contact lenses were worn in the same way and for the same periods as before. An apparatus was devised to measure the optical density of the guinea pig corneas. It consisted of an adaptation of the Model B Beckman Spectrophotometer, which supplied the light source and necessary measuring device. The animals were killed; the eye was rapidly dissected; the cornea plus a narrow scleral ring was removed and placed on a Lucite button which had an optically polished plane and convex surface; the latter was ground to a curve which fitted the internal surface of the cornea of the experimental animals. This button was mounted in a Lucite block which fitted precisely in a standard Beckman cuvette filled with 1.5% sodium bicarbonate solution. The corneas covered the plastic mount smoothly and adhered to it without mechanical aid, which might have induced tension or stress in the tissue. The light source at 400 mμ of the instrument was reduced to a pencil of light, 1 mm. in diameter, which passed through the cuvette, bicarbonate solution, center of the cornea, and Lucite button. The difference in the optical density of the cuvette, solution, and Lucite with and without the cornea was taken as the optical density of the cornea. The cornea and its support must be centered with care, for, owing to its curvature, a slight deviation causes considerable variation in the reading.

(*d*) *Corneal Thickness.*—The thickness was measured with a good machinist caliper (Browne and Sharpe Co. micrometer #13 RS) modified by adding a convex metal mount similar to the plastic button described above, to receive the cornea. The plunger of the caliper was pointed and the whole instrument mounted vertically before a slit lamp, so that the well-illuminated point of contact of the plunger with the cornea could be clearly observed with the microscope. The plunger of the micrometer did not press on the tissue. The micrometer could be read to 0.0001 in.; a series of readings taken in rapid succession were averaged for each determination.

In the experiments on turbidity and thickness, the animals were killed, the eyes removed and corneas



Effect of conventional contact lenses on the optical density, thickness, and water and lactic acid contents of the cornea of guinea pigs. In each case the lenses were worn on only one eye. Each point on the graph represents the average (four to six guinea pigs) ratio of the data obtained from the experimental and the control eye of the same animal. The data on optical density and thickness were obtained from the same corneas, and those on lactic acid and water content are based on a second group of animals.

Lactic Acid, Water Content, Optical Density, and Thickness of the Right and Left Corneas of Normal Guinea Pigs

Lactic Acid		Water Content					
LA		Mg. Wet Weight					
100 N_2		100 N_2		Optical Density		Thickness	
O. S.	O. D.	O. S.	O. D.	O. S.	O. D.	O. S.	O. D.
1.48	1.36	3.17	2.95	43	48	10.0	9.9
1.21	1.36	2.97	3.08	38	33	10.1	10.0
1.30	1.16	2.98	2.95	50	56	9.5	9.8
1.64	1.66	2.97	2.99	45	57	9.5	8.7
1.58	1.38	3.11	2.88	49	45	10.0	10.1
1.65	1.69	....	....	61	47	9.5	9.4
....	....	....	....	..	..	8.5	8.7
Mean							
1.47	1.42	3.03	2.97	47.6	47.6	9.56	9.51

fitted over the Lucite button, and the optical density determined. They were then removed, placed on the anvil of the micrometer, and the thickness measured. The measurements of the right, experimental eye were always compared with those of the left, control eye of the same animal. The variation which was found in water and lactic acid contents, turbidity, and thickness of the right and left corneas of normal animals is given in the Table.

RESULTS

The results of these experiments are shown in the Graph. The concentration of lactic acid in the cornea apparently begins to rise very quickly after the contact lens is in place, and continues to increase in amount throughout the experimental period. The values shown for the three- and four-hour periods were obtained from experiments in which the second cornea was not refrigerated while the first was being dissected, as in the other experiments; hence the values are no doubt slightly lower than they would have been had the final improved technique been used. The slight sag in the rising concentration curve is, therefore, not thought to be significant. The accumulation of lactic acid in the cornea clearly indicates a depression in the aerobic metabolism under the conditions of contact lens wear. A decrease in the corneal transparency also occurs coincident with the rise in lactic acid concentration. The curve of the ratios of the optical density (turbidity) of the normal and experimental corneas appears to be slightly different from the one showing an increase in lactic acid, although the magnitude of the response at six hours is essentially the same.

In order properly to interpret the change in optical density, it was necessary to determine the corneal thickness. This also was found to increase while contact lenses were worn, although the rate was not as great as that of the increase in optical density. The thickness measurements were made on the same excised corneas that were used for the optical density determination, so that such factors as tension or pressure on the corneal lamellae were comparable in both. An increase in the degree of hydration based on the ratio of the fresh corneal weight to its nitrogen content also was found. It, like the change in thickness, was not so marked as the increase in lactic acid content or optical density.

COMMENT

The concept that hydration and maintenance of the optical properties of the cornea depend on its metabolic activity,‡ and that the effect of contact lenses on corneal transparency and thickness is due to their interference with normal corneal aerobic metabolism has been set forth elsewhere.§ Conventional contact lenses, similar to those worn clinically, have been previously fitted to and worn by guinea pigs and shown to produce corneal clouding, which was observed subjectively. An increase in corneal thickness and hydration was demonstrated in these animals. Furthermore, the glycogen stores of the corneal epithelium were found to disappear after contact lenses had been worn a short time.[7] This suggested that the cornea suffered from relative anaerobic conditions which resulted in a higher rate of utilization of its carbohydrate and perhaps a slower rate of glycogenesis. If this conclusion was justified, one would expect to find an increase in the quantity of lactic acid in such corneas. This assumption was proved to be correct in the present experiments, which further emphasize the importance of metabolism in

‡ References 5 and 6.

§ References 1, 2, and 7.

regulation of the corneal water balance and hence of optical properties of the cornea. Langham [3] has clearly shown that the cornea in vivo exposed to an atmosphere of nitrogen does not respire at its normal rate, and that the relatively anaerobic condition thus induced results in an increase in its lactic acid content.

The ratio of the optical densities of the normal and experimental corneas apparently did not begin to rise as quickly as the lactic acid concentration. Whether this delay represents the true condition is questionable. The optical density of the control eyes generally was very consistent, there being a close agreement between the control values of all groups except those of the one-hour experiment. In these, the optical density of the normal cornea was high but without great variation within the group. If the high optical density of the control corneas in the one-hour group was indeed in error, then the ratio in this experiment should be higher and the curve of increasing optical density start earlier, as the general trend of the curve indicates.

The increase in optical density is obviously greater than the change in thickness; therefore, the transparency of a unit thickness of corneal tissue actually decreases, probably owing to disruption of the spacing of collagen fibers, and shifts in the index of refraction of the fluid around them. The change in thickness is very similar to that which occurs clinically, although measured by different methods.[8] The increase in corneal thickness presumably results from the inhibition of water; however, the thickness increased somewhat more than the water content. The cause of this discrepancy is not clear but may result from a slight elevation in acidity, which would increase the swelling. When the cornea is dissected for measurement, probably some thickening results from contraction of corneal fibers, thus shortening the corneal diameter and increasing its thickness. This contraction may have been accentuated in the experimental cornea due to its abnormal hydration and, perhaps, swelling of collagen fibrils induced by a shift in environmental pH.[9]

SUMMARY

That conventional contact lenses interfere with corneal metabolism is indicated by the increases in lactic acid which occur in the cornea when such lenses are worn. This results from the inability of the cornea to obtain the required O_2 from the atmosphere or palpebral mucosa when covered by an unventilated lens.

Concomitant increases occur in the optical density, thickness, and water content of the cornea, the last being responsible, at least in part, for the other two.

The increase in water content of the cornea is thought to result from an inhibition of its metabolic water-removing mechanism by the accumulation of lactic acid.

REFERENCES

1. Smelser, G. K., and Ozanics, V.: Importance of Atmospheric Oxygen for Maintenance of the Optical Properties of the Human Cornea, Science **115**:140, 1952.

2. Smelser, G. K.: Relation of Factors Involved in Maintenance of Optical Properties of Cornea to Contact-Lens Wear, A. M. A. Arch. Ophth. **47**: 328-343, 1952.

3. Langham, M.: Utilization of Oxygen by the Component Layers of the Living Cornea, J. Physiol. **117**:461-470, 1952.

4. Barker, S. B., and Summerson, W. H.: Colorimetric Determination of Lactic Acid in Biological Material, J. Biol. Chem. **138**:535-554, 1941.

5. Maurice, D. M.: Permeability to Sodium Ions of the Living Rabbit's Cornea, J. Physiol. **112**:367, 1951.

6. Potts, A. M.: Nutritional Supply of Corneal Regions in Experimental Animals: II. The Problem of Corneal Transparency and the Tonicity of Tears, Am. J. Ophth. **36**:127-138, 1953.

7. Smelser, G. K., and Ozanics, V.: Structural Changes in Corneas of Guinea Pigs After Wearing Contact Lenses, A. M. A. Arch. Ophth. **49**:335-340, 1953.

8. Kinsey, V. E.: An Explanation of the Corneal Haze and Halos Produced by Contact Lenses, Am. J. Ophth. **35**:691-695, 1952.

9. Bear, R. S.: The Structure of Collagen Fibrils, in Advances in Protein Chemistry, Anson, M. L., and others, Editors, Vol. VII, pp. 69-160, 1952.

Dependence of IOP-Lowering Effect of Acetazoleamide on Salt

V. EVERETT KINSEY, Ph.D.
ENRIQUETA CAMACHO, M.D.
GERARD A. CAVANAUGH, M.S., Detroit
MARGUERITE CONSTANT, St. Louis
and
DANIEL A. McGINTY, Ph.D., Detroit
With the Technical Assistance of June B. Twomey, B.S.

Acetazoleamide (Diamox) consistently produces a conspicuous fall in intraocular pressure when administered to patients with elevated ocular tensions, the magnitude of the response being less in persons with normal or slightly higher than normal pressures.* The administration of the drug to rabbits, however, is reported to produce a sizable reduction in pressure in a majority of animals † in some laboratories, but not in the eyes of most rabbits in others.‡ These discrepant results suggest that some environmental or endogenous factor acts to limit the reduction in pressure produced by acetazoleamide, so that the results of any study designed to investigate the mechanism of action of the drug may be more representative of the effect of the unknown variable than of the effect of acetazoleamide itself. Moreover, the discrepant observations make it difficult, if not impossible, to compare results obtained in different laboratories. Accordingly, we undertook an investigation designed to obtain, if possible, an explanation for the varied results. Some progress has been made in this connection, as we have found one possible extrinsic factor, dietary in nature, and one intrinsic factor, hormonal in nature, which appear in part to control the response to acetazoleamide. Because of the active interest in problems relating to acetazoleamide we feel it of value to publish at this time the results obtained to date.

From the Kresge Eye Institute, Detroit (Drs. Kinsey and Camacho, Mr. Cavanaugh, and Miss Twomey), supported in part by the Kellogg Foundation, Battle Creek, Mich.; Washington University School of Medicine, St. Louis (Dr. Constant), supported in part by Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y., and Parke, Davis & Company, Detroit (Dr. McGinty).

* References 1 and 2.

† Personal communications to the authors from Drs. J. S. Friedenwald, B. Becker, and W. M. Grant.

‡ Ballintine, E.: Personal communication to the authors.

The difference in response does not appear to be resolvable by differences in technique employed in measuring the pressure, or in the dosages of the drug used, since both of these factors were closely similar in all of the laboratories.

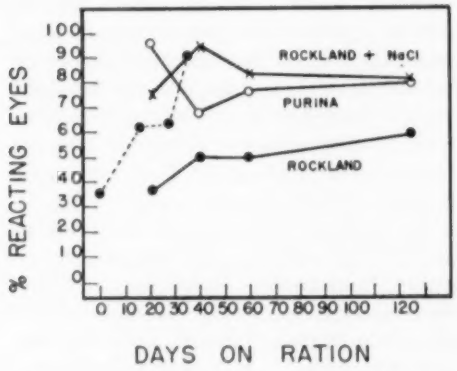
EXPERIMENTAL STUDY

It seemed probable that the differences in response were related to environmental rather than to genetic factors, since few laboratories use highly inbred strains of rabbits. Of the various environmental factors, diet was thought to be the most likely.

At the Wilmer Institute of Johns Hopkins Hospital, in Baltimore, and at the Washington University School of Medicine, where approximately 100% of the rabbits responded to acetazoleamide, the ration fed was, in the first instance, prepared by the Sherwood Company, of Baltimore, and, in the second, by the Purina-Ralston Company, in St. Louis. In the laboratory of the Kresge Eye Institute, where only about one-third of the rabbits tested responded to acetazoleamide, the ration fed was Rockland Rabbit Pellets, formulated by Rockland Farms, New

City, N. Y., and prepared by the Arcady Farms Milling Company, of Chicago.

It is apparent that if the ration employed was the factor determining the response to acetazoleamide, substituting the Purina for the Rockland ration would be expected to increase the proportion of "reacting" animals. An animal is classified as a "reactor" (i. e., one which responds to acetazoleamide positively) when the intraocular pressure is lowered by 3 scale divisions or more, as measured with a Schiøtz tonometer, using a 5.5 gm. weight, from 30 to 60 minutes after the intravenous administration of 100 mg/kg. body weight of acetazoleamide.



Percentage of eyes of rabbits, maintained for various periods on several rations, which responded to the action of acetazoleamide.

Accordingly, a preliminary experiment was performed in which the ration of three adult rabbits, selected because none of the eyes was shown to respond to acetazoleamide by lowered intraocular pressure (3 scale divisions), was changed from Rockland Rabbit Pellets to Purina Rabbit Chow Checkers. The animals were maintained on this ration for 26 days, at which time the standard dose of the drug was given and the eyes were retested. Four eyes responded positively. Another experiment, also of a preliminary nature, was performed with 14 additional rabbits. These animals had been maintained on a Rockland ration for several days after they had been received from local dealers. Ten of the 28 eyes responded to the drug at the start of the experiment. The broken line of the Figure shows the change in percentage of reacting eyes after the animals had been placed on a Purina ration for 16, 28, and 36 days. The percentage increased throughout the periods until about 90% of the eyes responded to the drug—a percentage greatly in excess of that which we had observed in stock animals maintained on Rockland ration.

The results of these initial experiments lent credence to the idea that some constituent in the Purina, but not in the Rockland, preparations might influence the response of the eyes to acetazoleamide.

The compositions, as cited by the manufacturers, of the two rations (Rockland and Purina), and also that of the Sherwood ration, were compared. The chief differences in them was the salt content, the percentages being 0.2, 0.5, and 1 for Rockland, Purina, and Sherwood rations, respectively.

The following controlled experiment was performed: Thirty-five young albino rabbits, whose average weight was 1300 gm., were divided into three groups, litter mates being distributed as equally as possible. The first group was fed the Rockland ration; the second, the Purina ration, and the third group, a special formulation of Rockland pellets prepared by the Arcady Farms Milling Company so as to contain essentially the same concentration of sodium chloride as the Purina ration. All of the animals were given water ad libitum.

Carefully sampled lots of the three rations were analyzed to determine the actual concentration of sodium chloride. The potassium chloride content, the ash pH, and the titratable alkalinity were also determined. The sodium chloride content was found to correspond closely to that cited by the manufacturers (Table 1). The analytical results also indicate that the titratable alkalinity of the Rockland Chow is considerably greater than that of the Purina Checkers, but, as will be evident, this does not seem to account for any difference in response of animals fed the two rations.

The percentages of eyes responding to acetazoleamide after the animals had been fed the several rations for varying periods are shown for each group by the three solid lines of the Figure. The percentage of eyes responding in the group of rabbits fed the special Rockland ration, i. e., the one containing additional sodium chloride, was essentially the same as that of rabbits fed the Purina ration. The percentage of reacting eyes of animals given the standard Rockland ration, however, was at all times less than that of the two other groups, although by the end of about five weeks it appeared to be greater than that found (28%, 18 of 64 eyes) in animals tested shortly after their arrival in the laboratory.

As mentioned previously, the results of the experiment described earlier, in which the ration was changed from Rockland to Purina, are also shown in the Figure (broken line). It will be observed that the percentage of reacting eyes in rabbits maintained on the Purina ration for approximately one month corresponded closely with that found when the animals were fed Purina pellets from shortly after weaning.

TABLE 1.—*Partial Analysis of Several Rations*

Ration	NaCl, %	KCl, %	Ash pH	Titratable Alkalinity*
Rockland	0.11	3.17	9.72	3.50
Rockland + NaCl	0.52	3.02	9.78	3.50
Purina	0.61	2.68	9.27	2.01

* Milliliters of 0.1 N HCl to phenolphthalein end-point on ash from 10 gm. ration.

Two other experiments which also seem to relate salt intake with the degree of ocular response to acetazoleamide were performed. In the first, 0.2% saline solution was substituted for drinking water. The five rabbits selected each consumed approximately 400 ml. of this fluid a day. At the end of 10 days the decline in pressure after acetazoleamide exceeded that observed while the animals were on plain water in 9 of 10 eyes, the average corresponding to 1.7 scale divisions.

In the second experiment, two rabbits whose eyes repeatedly were shown to respond with a change of 5 or more scale divisions when given acetazoleamide were sent to us from St. Louis by Dr. Becker. These animals had been fed a Purina ration and were kept in cages in which a salt lick was available. After arrival in Detroit they were tested several times and found to respond maximally to the drug. They were then placed on a Rockland ration for five weeks, at which time the average pressure change in the four eyes was reduced to below 3 scale divisions when again tested.

In an effort to relate the amount of response of the eyes to a difference in blood chemistry, analyses were performed to determine the concentrations of hydrogen ions, sodium, chloride, and total carbon dioxide. For this purpose only those animals were used which could be classified as reactors or nonreactors, depending on whether both eyes responded with a change of 3 or more scale divisions (reactors), or both eyes responded with a change of 2 or fewer scale divisions (nonreactors).

The analyses for sodium and chloride were performed in triplicate on pooled samples of plasma from animals maintained for about three months on each of the three aforementioned dietary regimens, and those for total carbon dioxide and pH were performed on individual samples of plasma and whole blood, respectively.

The hydrogen ion concentrations of whole blood before and 16 days after the rations of 14 animals (both reactors and nonreactors) had been changed from Rockland to Purina are shown in Table 2. There is no significant difference between the pH of the blood of reactors and that of nonreactors fed Rockland ration. The blood from reacting animals fed Purina ration was slightly more alkaline than that from the nonreactors fed the same ration. Because of the few animals involved, however, and additional results shown in Table 3, which indicate that no appreciable difference exists in the pH of the blood of other reacting and nonreacting rabbits, it is concluded that the blood pH is not a determining factor so far as ocular response to acetazoleamide is concerned.

TABLE 2.—*Hydrogen Ion Concentration of Blood of Rabbits Initially Fed Rockland Rabbit Ration and Then Transferred to Purina Ration for Sixteen Days, Classified as to Whether Both Their Eyes Responded to Acetazoleamide*

Classification of Animal	Ration Fed: Rockland pH (Av.)	Rockland pH Range	Purina pH (Av.)	Purina pH Range
Reactor.....	7.24 (5) *	7.15-7.33	7.32 (9)	7.18-7.45
Nonreactor....	7.22 (9)	7.15-7.28	7.22 (4)	7.12-7.32

* Figures in parentheses represent number of rabbits.

TABLE 3.—*Concentration of Sodium, Chloride, Total Carbon Dioxide in Plasma, and Hydrogen Ion Concentration in Whole Blood of Rabbits, Classified As to Whether Both Their Eyes Responded to Acetazoleamide*

Classification of Animal	Na,* mM./Kg. Water	Cl, mM./Kg. Water	Total CO_2, mM./Kg.	pH
Reactor.....	145 (11) †	118 (11)	18 (9)	7.31 (9)
Nonreactor..	148 (7)	122 (7)	21 (6)	7.33 (6)

* Analyses performed by Miss Margaret Rourke, of Massachusetts General Hospital, Boston.
† Figures in parentheses represent number of rabbits.

The concentrations of sodium, chloride, and total carbon dioxide in plasma, and that of hydrogen ions in whole blood, of reacting and nonreacting animals are shown in Table 3. The differences in concentration of the substances tested appear to be so small as to fall within the analytical and animal-to-animal variation and thus to be unrelated to whether or not the animal was a reactor.

Neither was it possible to relate the acetazoleamide response of the eyes to the average weight gain, or the initial intraocular pressure. Thus, the average weight gain during 60 days on the Rockland ration with added salt was 206%, as compared with 205% when standard Rockland ration was fed; yet at the end of 60 days the percentages of reacting eyes were 83 and 50 for the two groups, respectively. Furthermore, the initial pressures for both the 34 reacting eyes and the 18 nonreacting eyes were identical. Incidentally, the sex of the animal appeared also to be without influence on the response.

In view of the apparent dependence of the intraocular pressure response of rabbits to acetazoleamide on dietary sodium chloride,

TABLE 4.—*Effect of Aldosterone in Increasing the Pressure-Lowering Response of Rabbit Eyes to Acetazoleamide* *

Animal	Dose Aldosterone, γ	0 Min. O.S.	0 Min. O.D.	30 Min. O.S.	30 Min. O.D.	90 Min. O.S.	90 Min. O.D.	Maximum Change O.S.	Maximum Change O.D.
N	0	4	4	6	7	6	7	2	3
N	0.5	5	5	7	8	8	9	3	4
O	0	3	3	5	5	5	5	2	2
O	0.5	4	4	8	9	7	8	4	5
P	0	2	2	4	4	4	4	2	2
P	0.5	3	3	8	8	6	5	5	5
R	0	4	4	6	7	6	6	2	3
R	0.5	4	4	7	7	8 (60 Min.)	8 (60 Min.)	4	4
E	0	2	2	4	4	3	3	2	2
E	1.0	2	2	6	6	5	6	4	4
F	0	2	2	3	3	2	3	1	1
F	1.0	2	2	6	7	5	6	4	5
P	0	2	2	4	4	4	4	2	2
P	1.0	2	3	6	7	6	7	4	4
R	0	2	2	4	3	4	4	2	2
R	1.0	2	2	4	5	4	5	2	3
S	0	3	3	5	5	4	5	2	2
S	5.0	2	2	5	6	5	5	3	4
U	0	2	2	4	4	3	3	2	2
U	5.0	2	2	5	5	4	4	3	3
				Average: Acetazoleamide alone				1.9	2.1
				Acetazoleamide with aldosterone				3.6	4.1

* The values are expressed in scale units of a Schiötz tonometer (5.5 gm. weight).

it appeared worth while to inquire as to whether increasing the salt retention of animals by administration of salt-retaining steroid hormones might likewise increase the responsiveness. For this purpose the adrenal corticoid aldosterone, which has been shown recently to be the most effective of the salt-retaining hormones, was selected for the first trials.

Ten rabbits the majority of whose eyes had been shown to respond relatively poorly to acetazoleamide were retested in the usual manner and the following day were given an intramuscular injection of aldosterone § 60 minutes prior to another test dose of acetazoleamide. The results are shown in Table 4, where it may be seen that in every instance but one the response was greater in those animals receiving aldosterone. The average change for all eyes with acetazoleamide alone corresponded to 2 scale divisions, whereas with aldosterone in addition to acetazoleamide the change corresponded to almost 4 scale divisions. In other words, the rabbits were changed from nonreactors to reactors. Similar results were obtained with other salt-retaining hormones, such as DOCA and 9-alpha-fluorohydrocortisone. These results will be presented in a subsequent paper.

On the basis of the results obtained with the exogenous use of the salt-retaining hormones, 10 milliunits of corticotropin in water was injected into each of four animals, all of whose eyes were nonreacting. The eyes remained nonreacting when tested in the usual manner. This experiment was repeated using 500 milliunits of corticotropin. In this instance two of eight eyes reacted to acetazoleamide. Five units of corticotropin in gelatin was then given daily for six days to six nonreacting rabbits. At the end of this period 4 of the 12 eyes were observed to respond.

COMMENT

The results considered together, while not of an all-or-none nature, suggest that salt intake over a period of some weeks influences the ocular response to acetazoleamide. Those obtained with aldosterone were much more striking in that the administration of extremely small doses of this corticoid converted almost every nonresponsive eye to a responsive one (19 of 20) within several hours after the hormone was given. Corticotropin was much less effective, since only when given repeatedly was there any suggestion of influence on the drug response.

That it was the content of salt of the different rations that altered the response, rather than some other constituent, is suggested by the experiment in which salt was the only factor varied (Rockland *vs.* Rockland + added salt), and that it was the sodium rather than the chloride is at least suggested by the knowledge that aldosterone is known to promote increased reabsorption of sodium rather than chloride.

The mechanism by which increased salt intake acts to change the response to acetazoleamide is not apparent. It will be recalled that there was no significant difference in the concentration of sodium or chloride in the plasma of animals whose eyes were refractory to acetazoleamide, nor was there any apparent difference in either total carbon dioxide content or pH. It may be that the intracellular salt content was higher in those animals subsisting on rations with elevated salt content; nevertheless, it is not clear how this should affect the response to acetazoleamide.

The mechanism by which aldosterone influences the reaction to acetazoleamide is also obscure. Since the effect of the hormone was manifest within one to two hours after administration, it seems unlikely that the response could have occurred as a result of any gross retention of sodium by the kidney. Moreover, the acute injection in nonreacting rabbits of amounts of sodium chloride far in excess of that which could be retained by the kidney in a matter of one or two hours did not transform the animals into reactors.

While it is not apparent how either increased sodium intake or aldosterone acts to potentiate the effect of acetazoleamide, the

§ The aldosterone used in these experiments was supplied by Prof. T. Reichstein, of Basel, Switzerland.

question still arises as to whether their action may not be interdependent. Axelrad and associates,[3] for example, have shown that the excretion of aldosterone increases with reduction of sodium intake, and Peschel and Race [4] have shown that in rats, and in some patients, reduced sodium intake or excessive potassium intake results in a sizable increase in the width of the zona glomerulosa of the adrenal, with reduction in cytoplasmic lipids, whereas with elevated sodium intake this layer decreases in width. These observations are interpreted to mean that the amount of hormone production rises with lowered, and falls with increased, salt intake. Their results, assuming the correctness of their interpretation, would be diametrically opposed to the idea that increased sodium intake increases the response of rabbits to acetazoleamide by increasing the endogenous supply of aldosterone or other salt-retaining hormones.

An interpretation which would seem to bring all of the results into agreement is either that lowered sodium intake impairs the utilization of aldosterone or that it prevents retention of the hormone. In view of the several instances in which the effect of the sodium-retaining hormone DOCA, for example, is known to be modified by the absence of adequate salt in the diet, perhaps it is not too unlikely a proposition that the hormone is required to retain sodium, just as sodium is required to retain the hormone.

In any event, it seems probable that there is, as in other organs, such as the kidney, a common basis for the effects produced in the eye by elevated salt intake and the sodium-retaining hormone.

SUMMARY

The proportion of eyes which responded with a significant decrease in intraocular pressure ‖ after intravenous administration of acetazoleamide (100 mg/kg. of body weight) was shown to depend upon salt intake over a period of some weeks.

Approximately 90% of eyes of animals subsisting on a ration containing 0.5% sodium chloride responded positively, as compared with about 40% to 50% of eyes of animals subsisting on a ration containing 0.2% sodium chloride.

Ninety-five per cent of eyes demonstrated to be unresponsive to acetazoleamide were made to respond by parenteral injection of from 0.5γ to 5.0γ of the salt-retaining mineralocorticoid aldosterone.

Approximately one-third of nonreacting eyes were made to react after six daily intramuscular injections of 5 units of corticotropin, but no significant increase in response was noted after the acute administration of ½ unit of corticotropin.

The effect of increased salt intake on the response to acetazoleamide could not be related to plasma sodium, chloride, total carbon dioxide, or blood hydrogen ion concentration.

The possible common mechanism of action of increased sodium intake and aldosterone is discussed in the light of other known interrelations between these two factors.

‖ Three scale divisions as measured with a Schiøtz tonometer, using a 5.5 gm. weight.

REFERENCES

1. Becker, B.: Decrease in Intraocular Pressure in Man by a Carbonic Anhydrase Inhibitor, Diamox: A Preliminary Report, Am. J. Ophth. **37**:13, 1954.

2. Grant, W. M., and Trotter, R. R.: Diamox (Acetazoleamide) in Treatment of Glaucoma, A. M. A. Arch. Ophth. **51**:735, 1954.

3. Axelrad, B. J.; Cates, J. E.; Johnson, B. B., and Luetscher, J. A.: Aldosterone in Urine of Normal Man and of Patients with Oedema: Its Increased Recovery After Hydrolysis with Acid and with Beta-Glucuronidase, Brit. M. J. **1**:196, 1955.

4. Peschel, E., and Race, G. J.: Studies on the Adrenal Zona Glomerulosa of Hypertensive Patients and Rats (with Special Reference to the Effect of Dietary Salt Restrictions), Am. J. Med. **17**:355, 1954.

Reduced Ocular Tension After Cataract Surgery

A. C. HILDING, M.D., Ph.D., Duluth, Minn.

Ocular tension is commonly reduced below normal for some time after cataract extraction. If one interested in postoperative hypotony peruses the literature on the subject, he is left with a number of unanswered questions. Is the hypotony following lens extraction of importance? How regularly does it occur? To what is it due? Does it cause complications? If the ophthalmic surgeon could have available to him a graph picturing the predicted intraocular tensions following cataract surgery, similar to that published by Kronfeld [20] in his study following withdrawal of aqueous humor, he might feel that he could assess the postoperative course of his cataract patients more effectively.

The term hypotony is used by some writers to indicate a tension of 10 or below. In this article, the term hypotony will be used to indicate any subnormal tension.

LITERATURE

A number of studies have been made on hypotony following operation for glaucoma. Fanta,[7] Vannas and Björkenheim,[33] O'Brien and Weih,[28] and McPherson [22] all discuss that which follows cyclodialysis. Van Heuven [32] found hypotony after cyclodiathermy, and Gifford [12] reports one instance after iridectomy alone. Fistulization operations for glaucoma may bring about such severe hypotony * that it becomes necessary to reduce the filtering bed in order to control it.

Nonperforating injuries, such as blows upon the eye from a fist, balls, or other blunt objects, may be followed by hypotony which may continue for as long as a year or two. Myopia is often a complication under these circumstances.† This type could be related to that which follows cataract operation. Perforating injuries, as anticipated, are followed by hypotony.‡ Heath [13] reviewed the entire subject of hypotony some years ago and in that review discussed briefly hypotony following cataract operation. Bhat [2] cites a case of ophthalmomalacia following cataract extraction, in which hypotony was a prominent symptom. Dunnington and Regan [6] describe a series of cases of unintentional fistulization from trauma or operation, accompanied by severe hypotony. Kirby § gives hypotony as one of the causes of failure of cataract operation. He feels that manipulation over the sclera, ciliary body, and cornea is a factor in the production of detachment of the choroid and indirectly of the associated hypotony. It is his feeling that ocular hypotony is a serious sign in trauma of the eye.

PRESENT STUDY

The present study was undertaken for the purpose of clarifying the role of hypotony after cataract surgery. One hundred thirty-four eyes were measured with a tonometer from one to five times during the convalescent period; 322 of the readings made were included in these data.

Work done in the Research Laboratory, St. Luke's Hospital, under grants by the Louis W. and Maud Hill Family Foundation of St. Paul, the Edward C. Congdon Memorial Trust, Miss Elisabeth Congdon, and the Women's Service Guild of St. Luke's Hospital.

* References 1, 4, 5, and 36.

† References 8, 13, 14, and 34.

‡ References 6, 13, and 14.

§ References 17 and 19.

Two hundred ninety-five determinations of the tactile tension taken between the 9th and 17th days were recorded and graphed. The determinations were placed in five categories: normal, low normal, low, soft, and zero. However, it was felt that the results could be so inaccurate and subjective as to be of little scientific value, and they are omitted from this report. As a matter of fact, in general they did parallel the tonometric readings rather strikingly.

One-tenth cubic centimeter of air was injected into the anterior chamber at the conclusion of operation in 40 of the eyes included in this study, to see if the rate of absorption would give some clue to the rate of aqueous production and to the course of the postoperative tension.

The tension determinations were all made with the same instrument, a standard McLean tonometer. This instrument is not graduated below 10, and there is a stop on it which prevents further deviation of the needle at approximately the point where 0 pressure would be located. As a consequence, those which were listed at less than 10 were all grouped at 5, and those in which the needle rested against the stop were all grouped at 0. This would account for a grouping of readings at these two points in some of the graphs. The anesthetic used was 0.5% tetracaine (Pontocaine) hydrochloride

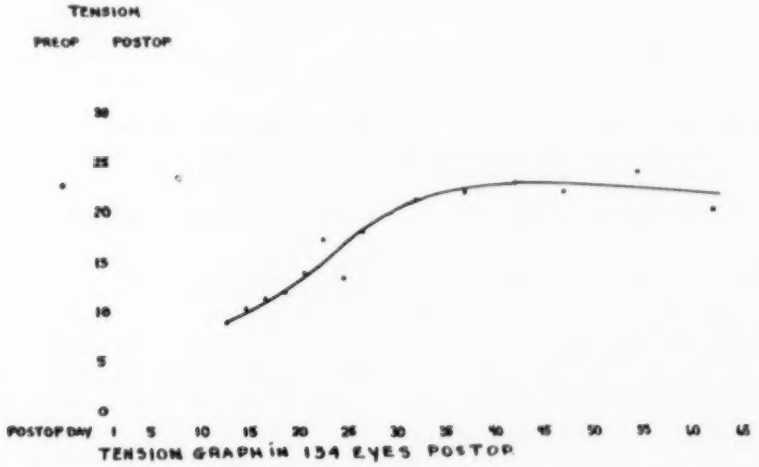
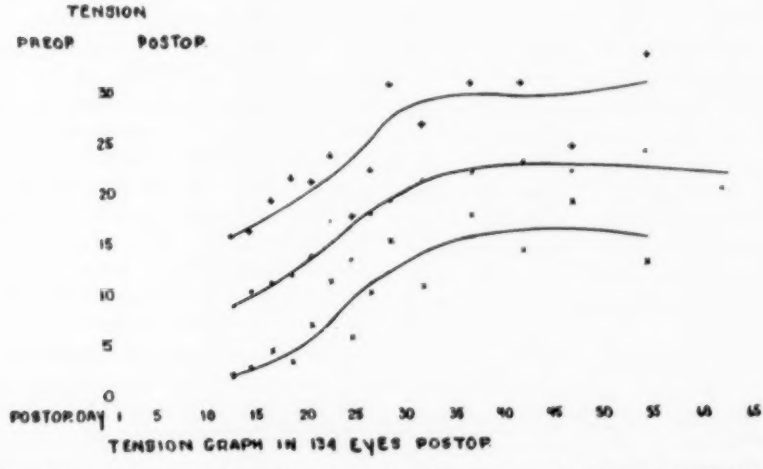
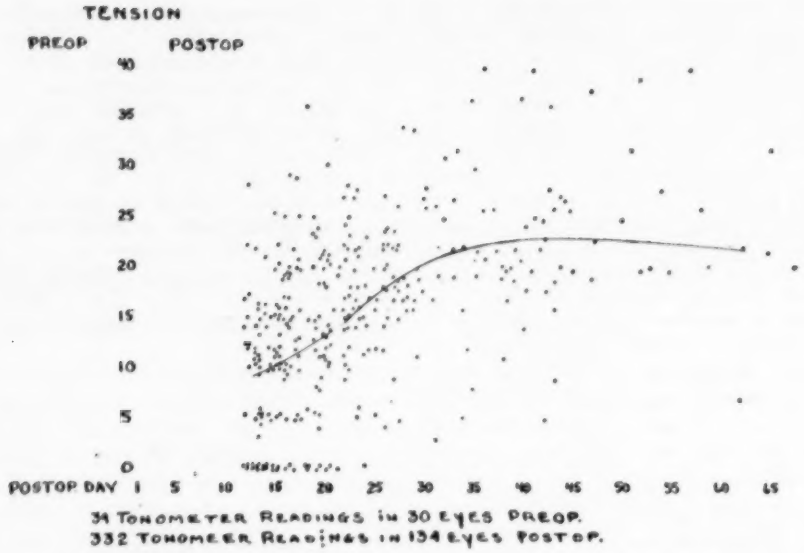


Fig. 1.—(*A*) Arithmetic mean of 332 postoperative tonometric readings in 134 eyes.



(*B*) The central curve is the same as in *A*; the other two curves indicate the standard deviations calculated for 48-hour periods.



(*C*) A scattergram of all 332 readings with the arithmetic mean superimposed lightly.

The tension was not taken with the tonometer before the 12th day. After the 12th day, it was repeated at irregular intervals during the postoperative period. No determinations were made unless the anterior chamber was completely formed and of aphakic depth. Preoperative determinations were secured upon 30 of the eyes and found to vary somewhat more widely than is the case in perfectly normal eyes.

FINDINGS

The findings yielded by the eyes studied lend themselves to this concise statement: A reduced postoperative tension after the 12th day was generally present.

The graph of the arithmetic mean of the determinations made is shown in Figure 1*A*. Doubtless a much larger number of measurements would show an almost identical curve. But when the standard deviations are worked out (Fig. 1*B*), one must wonder if the arithmetic mean alone gives a great deal of information as to what can be expected in any individual case. The standard deviations are wide, and the probable error in any given case would be large. A scattergram (Fig. 1*C*) shows quite a general distribution of measurement from 0 up to normal. But this also fails to give a picture of what is to be expected in any individual case or small group of cases. It would be quite possible, as far as the scattergram is concerned, that all or most of the very low readings were found in a comparatively small number of eyes and all of the high readings in another group, and that the small group of eyes with low readings could bring down the arithmetic mean of the group as a whole to show a curve such as that in Figure 1*A*.

To test this possibility, 35 eyes, which showed a low tension (10 or less) between the 12th and 16th day, were grouped together and a separate graph of the arithmetical mean and scattergram made of this group. One hundred sixteen determinations from this group are illustrated in Figure 2. It will be seen that the distribution of all of the readings in these eyes is very much like that of the group as a whole. The mean curve is similar except that it is at a somewhat lower level and rises somewhat more steeply. This would indicate that the mean reduction of pressure after operation is not due to a small group with especially low tension. Most eyes share in it.

Some hold to the opinion that the reduction of intraocular pressure after operation is always, or usually, due to leakage of the

operative wound. It so happened that during the time this study was made a certain type of suture (no longer used) was employed. Following its removal, the anterior chamber collapsed not infrequently. For the purposes of this study, it was assumed that all eyes had leaked in which the anterior chamber was found to be empty the day after the suture removal. It was further assumed that those in which the anterior chamber did not form for several days, or in which the anterior chamber collapsed after it had once been formed, were also leaking. When these three categories were combined into a group, it contained 37 eyes. The tensions in this group were recorded after the wounds were judged to be well healed and after the anterior chambers had re-formed to aphakic depths. This group is shown in Figure 3. The mean curve is a little higher than in that

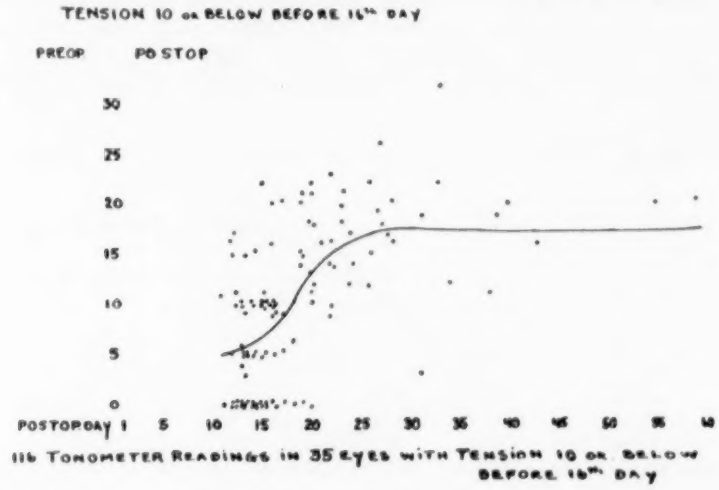


Fig. 2.—Scattergram and arithmetic mean of 116 tonometric readings in 35 eyes in which a tension below 10 was found at least once between the 12th and 16th days.

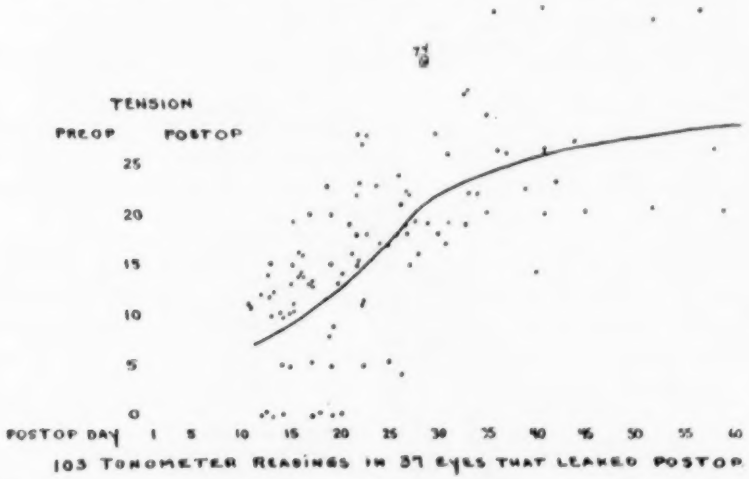


Fig. 3.—Scattergram and arithmetic mean of 103 tonometric readings in 37 eyes that were presumed to have leaked sometime before the 12th day but were not leaking when the measurements were made.

for the group as a whole, and the scattergram shows a number of comparatively high readings. One eye developed a frank glaucoma and reached a tension of 74. But, in general, the course of postoperative tension did not differ a great deal from the group as a whole. It is to be expected that the readings in this group would be somewhat higher, because some degree of formation of anterior synechiae must have occurred in a number during the period when the chamber remained empty.

Figure 4 shows the curves of the three above-described groups superimposed.

A and *B* of Figure 5 depict the graphs of the tension of 31 individual eyes in which four or more determinations were made during the period included in the study. Figure 5*A* represents a consecutive group of 20 such eyes and *B* the next 11 taken consecutively (graphed separately for greater visibility). Looking at these figures, one sees perhaps a truer picture of postoperative hypotony than on any of the previous graphs or scattergrams. It will be noted at once that there is no regular pattern; 12 out of the 31 show a steeply rising course, and, oddly enough, nearly all of these occur in the first 20. Very

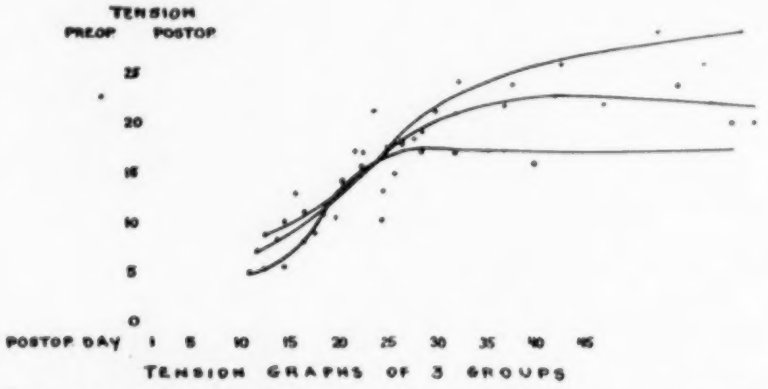


Fig. 4.—Curves of the arithmetic means of the three groups superimposed, namely, the group as a whole, the group which leaked, and the lowest tension group.

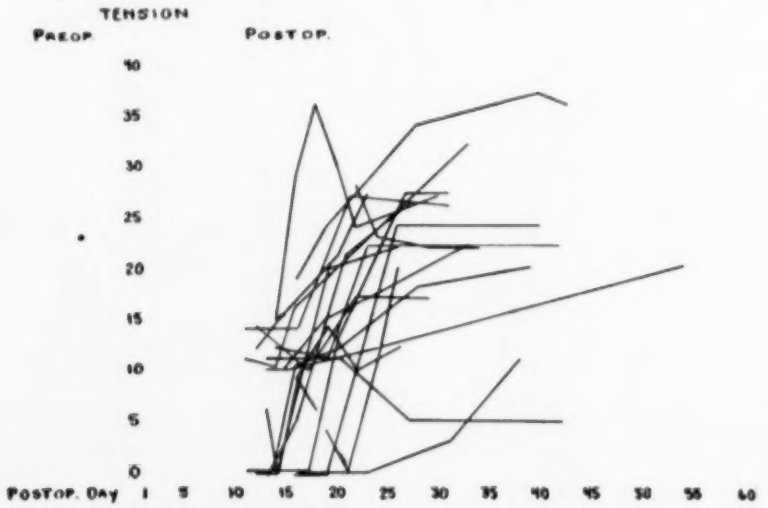
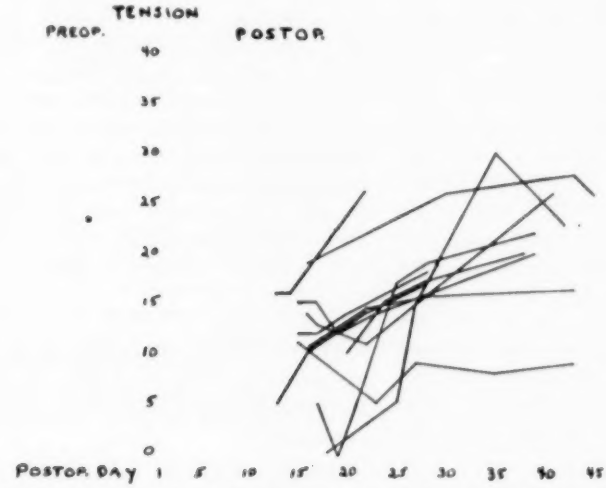


Fig. 5.—(*A*) Individual graphs of 20 eyes in which four or more determinations were made.

few among the first 20 show a graph which is at all like the arithmetic mean of the 332 readings on the 134 eyes studied. However, the next 11 eyes several parallel this curve roughly. Some eyes, it will be seen, recorded a tension of 0 as late as three weeks postoperatively, despite the fact that the anterior chamber was fully re-formed. In many eyes, once the ocular tension started to rise, it showed a tendency to reach normal levels within a period of three to five days. Only a few remained low for a long period of time. The steep rise toward normal was found to begin on any day from the 12th to the 22d. This fact, that the rise begins at different times, obscures the nature of the rise when a number are averaged. If all of the eyes followed this pattern of a steep rise from 0 to normal values and thereafter a plateau, the arithmetic mean would, nevertheless, show a curve somewhat like that seen in Figure 1, since the beginning of the rise occurs on different days. In other words, the average of a large group in this study tends to obscure, rather than clarify, the picture of what actually happens.



(*B*) Individual graphs of 11 more eyes in which four or more determinations were made.

AIR BUBBLE

One-tenth cubic centimeter of air was injected, at the conclusion of the operation, into 40 of the eyes in this study, and an attempt was made to see if the rate of disappearance of the bubble bore any relationship to the postoperative tension. The bubble was last seen on the first postoperative day in two eyes; i. e., the bubble was gone by the second postoperative day. It was last seen on the second postoperative day in 1 eye, on the third in 7 eyes, on the fourth in 14 eyes, and on the fifth postoperative day in 16 eyes. No bubble was seen as late as the sixth postoperative day in any of these 40 eyes. No correlation could be established between the time required for the bubble to absorb and the course of the postoperative tension.

VISUAL RESULTS

The visual results were determined in the three groups, i. e., the group as a whole, the low-pressure group, and the eyes which leaked. Vision of 20/30 or better was attained in 68.4% of 130 eyes in the group as a whole. This compares with 68.1% of 20/30 or better in a larger series of 370 eyes presently under analysis. Of 35 eyes in the low-pressure group, 76.6% attained 20/30 or better and 70% of the 37 with leaks showed this degree of vision. It is, of course, not to be presumed that better vision may be obtained in the eyes with an exceed-

ingly low postoperative tension or leak. The better average result obtained in these groups is doubtless a variation due to chance, and of no statistical significance.

COMMENT

Reduced postoperative ocular tension was found in nearly all of the 134 eyes studied during the postoperative period after the 12th day. Presumably the tension was 0 or close to it in the days immediately following operation, but no determinations were made at this time. No serious complication from hypotony seemed to result in any instance. What, if any, effect the low tension had on the final visual result is conjectural because the hypotony was so general that there were few eyes with which to make comparison. The postoperative tension may remain very low up to three weeks. Judging by the individual graphs in Figure 5, somewhat less than half the eys, if similarly graphed, might have shown an increase in the tension to near-normal levels within a few days after it started to rise. The rise, as found, began on any day up to the 22d. The postoperative course of the ocular tension, although generally low, was irregular. There was no general pattern. The visual result was uniformly good, and by no means worse in those eyes which exhibited the lowest tension.

The cause of the hypotony is not clear. It does not seem likely that it is due to leak. By and large, the incisions were all smoothly healed. The anterior chamber was deep in all, and nothing could be found by corneal microscope indicating leak. The group which had had empty chambers prior to taking of tension followed a course similar to that of the group as a whole after the chamber had refilled.

It is a common experience to encounter hypotony of considerable duration following a blow upon the eye, and it may not necessarily be a very severe blow. Presumably the injury from such a blow is due to the action of changes of pressure and deformation upon the ciliary body, and perhaps also upon the iris, choroid, and filtration angle. One cannot presume that surgical manipulations of the magnitude of those incidental to cataract surgery would be without effect upon these structures. Little information is available concerning operative trauma to the ciliary body. Trauma, accompanied by edema or hemorrhage (or both), might very well follow external manipulations or the traction incidental to tearing of the zonule. Hemorrhages and edema with disturbance of electric potentials between the stroma and the epithelium and disturbance of filtration might reduce the production of aqueous, and the general congestion might enhance the rate of outflow. It would not be unthinkable that hemorrhages into the ciliary body could recur during the postoperative period. It seems to me that the cause of postoperative hypotony likely lies here. It might be very similar to the cause of hypotony following blows upon the eye. As the ciliary body recovers from the trauma and begins to function normally, and the outflow to come under physiologic control, balance, with a normal tension, is again attained.

SUMMARY

Postoperative hypotony following cataract extraction is still present after the 12th day so regularly that it is the rule and is to be expected.

The results of this study do not indicate that the hypotony is apt to cause complications. The visual results are generally good despite low tensions, sometimes sustained for several weeks. The cause of the hypotony has not been determined, but likely lies in trauma to the ciliary body, filtration angle, or iris, individually or in combination.

REFERENCES

1. Barkan, H.: Use of the Shahan Thermophore in Hypotony of the Eyeball as a Result of the Elliott Trephining Operation, Am. J. Ophth. **23**: 692-693 (June) 1940.

2. Bhat, P. K.: Hypotony Following Cataract Extraction, Antiseptic **42**:45 (Jan.) 1945.

3. Brittain, I., and Brittain, G. J. C.: Unilateral Hypotony During Anesthesia, Brit. M. J. **1**:442-444 (March 31) 1945.

4. DeVoe, A. G.: A Gonioscopic Study of Fistulizing Operations, A. M. A. Arch. Ophth. **46**:504-509 (Nov.) 1951.

5. Duke-Elder, S.: Fundamental Concepts in Glaucoma, Arch. Ophth. **42**:538-545 (Nov.) 1949.

6. Dunnington, J. H., and Regan, E. F.: Late Fistulization of Operative Wounds, Arch. Ophth. **43**:407-418 (March) 1950.

7. Fanta, H.: Ocular Hypotony Due to Vitreous in Cyclodialysis Pocket, Ophthalmologica **118**:205-207 (Sept.) 1949.

8. Fox, S. A.: Traumatic Myopia with Hypotony: Report of 2 Cases with Review of the Literature, Arch. Ophth. **28**:218-234 (Aug.) 1942.

9. Friede, R.: Treatment of Chronic Hypotonia Bulbi, Wien. klin. Wchnschr. **59**:752-754 (Nov.) 1947.

10. Friedenwald, J. S., and Stiehler, R. D.: Circulation of the Aqueous: VII. A Mechanism of Secretion of the Interaocular Fluid, Arch. Ophth. **20**:761-786 (Nov.) 1938.

11. Friedenwald, J. S., and Stiehler, R. D.: Formation of Intraocular Fluid and Permeability of the Ciliary Body, Proc. Soc. Exper. Biol. & Med. **34**: 447-448 (May) 1936.

12. Gifford, S. R.: Treatment of Secondary Glaucoma, Arch. Ophth. **23**:301-315 (Feb.) 1940.

13. Heath, P.: Ocular Hypotony, Tr. Am. Acad. Ophth. **52**:613-621 (July-Aug.) 1948.

14. Heath, P.: On Ocular Hypotony, Am. J. Ophth. **31**:1317-1318 (Oct.) 1948.

15. Igersheimer, J.: Intraocular Pressure and Its Relation to Retinal Extravasation, Arch. Ophth. **32**:50-55 (July) 1944.

16. Kinsey, V. E., and Grant, W. M.: Secretion-Diffusion Theory of Intraocular Fluid Dynamics, Brit. J. Ophth. **28**:355-361 (July) 1944.

17. Kirby, D. B.: Causes of Failure of Cataract Operations, Am. J. Ophth. **37**:87-98 (Jan.) 1954.

18. Kirby, D. B.: Ocular Hypotony, Am. J. Ophth. **23**:812-813 (July) 1940.

19. Kirby, D. B.: Prevention and Handling of Complications Arising During and After Cataract Extraction, Arch. Ophth. **25**:863-901 (May) 1941.

20. Kronfeld, P. C.: Ocular Phenomena Elicited by Withdrawal of Aqueous Humor, Arch. Ophth. **28**:552-556 (Sept.) 1942.

21. Matteucci, P., and Kluzer, G.: Relationship Between Glaucomatous Cupping, Ocular Hypertension and Pressure of the Cerebrospinal Fluid, Atti 37 Congr. Soc. oftal. ital. **10**:559, 1948; abstracted ,Am. J. Ophth. **33**:1958, 1950.

22. McPherson, S. D., Jr.: Cyclodialysis in the Treatment of Glaucoma, Am. J. Ophth. **29**:848-853 (July) 1946.

23. O'Brien, C. S., and Weih, J.: Cyclodialysis, Arch. Ophth. **42**:606-619 (Nov.) 1949.

24. Ortiz, J. M. V.: Intraocular Pressure in Cases of Hemorrhage of the Retina, Arch. Ophth. **39**:661-664 (May) 1948.

25. Pillat, A.: Intracapsular Extraction of Cataracta Complicata Accreta After Iridocyclitis and Glaucoma, Arch. Ophth. **42**:567-582 (Nov.) 1949.

26. Poos, F.: Über die drucksenkenden Faktoren bei der sog. osmotischen Hypotonie, Klin. Monatsbl. Augenh. **89**:145-170 (Aug.) 1932.

27. Rednót, M.: Origin of Hypotony of the Eye: Ocular Findings in Orthostatic Hypotony, Klin. Monatsbl. Augenh. **109**:161 (March-April) 1943.

28. Sondermann, R.: Relationship Between Intraocular Pressure, Pressure in the Retinal Vessels and Pressure of the Spinal Fluid, Klin. Monatsbl. Augenh. **114**:161-168, 1949.

29. Sondermann, R.: Physiology and Pathology of Intraocular Pressure, Klin. Monatsbl. Augenh. **112**:113-124, 1947.

30. Strampelli, B.: Retrobulbar Cocaine Injection to Produce Hypotony, Atti 37 Congr. Soc. oftal. ital. **101**:336-339, 1948; abstracted, Am. J. Ophth. **33**: 1651, 1950.

31. Troncoso, M. U.: Use of Tantalum Implants for Inducing Permanent Hypotony in Rabbits' Eyes, Am. J. Ophth. **32**:499-508 (April) 1949.

32. Van Heuven, J. A., and Dunn, J. P.: Correlation of Intraocular Pressures, with Microscopic Sections Following Cyclodiathermy on Normal Rabbits, Am. J. Ophth. **36**:1447-1449 (Oct.) 1953.

33. Vannas, M., and Björkenheim, B.: On Hypontony Following Cyclodialysis and Its Treatment, Acta ophth. **30**:63-64, 1952.

34. Weekers, R.: Myopia and Traumatic Hypotony, Ann. ocul. **178**:236-241 (June) 1945; abstracted, Am. J. Ophth. **29**:772 (June) 1946.

35. Wheeler, J. M.: Conjunctival Plastic Operation for Hypotony Following Filtering Operations, in The Collected Papers of John Martin Wheeler, M.D., on Ophthalmic Subjects, New York, Columbia University Press, 1939, p. 421.

36. Workman, J. B., Jr.: Conjunctival Plastic Operation in Cases of Hypotonia from Filtering Operations on Ocular Fistulae, J. South Carolina M. A. **37**:249-250, 1941.

The Fields of Vision and Their Significance When Projected into Space

H. S. WELSMAN, M.D., Guelph, Ont., Canada
and
CLEMENT McCULLOCH, M.D., Toronto, Canada

The fields of vision are tested clinically by using a chosen working distance and by varying the size of the test object. This method is convenient and by custom has become part of the practice of ophthalmology. However, this scheme of testing, and the mathematical analysis which obviously results, leads to a fallacious understanding of the limits of visual space.

The error arises from the fact that in daily experience observers are not considering objects which vary in size, but are concerned with objects which remain constant in size and vary in distance. A baseball does not grow or shrink in size; it comes nearer or goes away. The size of the visual field for a given object varies with the apparent size of the object, which is a function of the distance of the object from the observer. The mushroom-shaped island of vision so often reproduced from the data of Roenne [1] (Fig. 1) has little relation to reality. Rather, the figure should be redrawn, assuming that the object has constant size but is varying in distance from the observer.

We have tested the fields of vision using different brightnesses, different contrasts, and different sizes of test objects. The results of this work have been recalculated, assuming that the size of the test object remains constant but that the working distance varies. The figures so obtained represent the field of vision for a given, standard object viewed at all possible distances from the observer. When calculated in this manner, the fields of vision look entirely different from those commonly presented in the textbooks.

From Institute of Aviation Medicine, R. C. A. F., and Department of Ophthalmology, University of Toronto.

LABORATORY PROCEDURES

Fields of vision were taken on a tangent screen in much the same manner as they are done clinically. Dark test objects were used against a white background. The working distances varied from 2000 to 10,000 mm.; the brightness of the screen, from 6 to 822 ft-c.

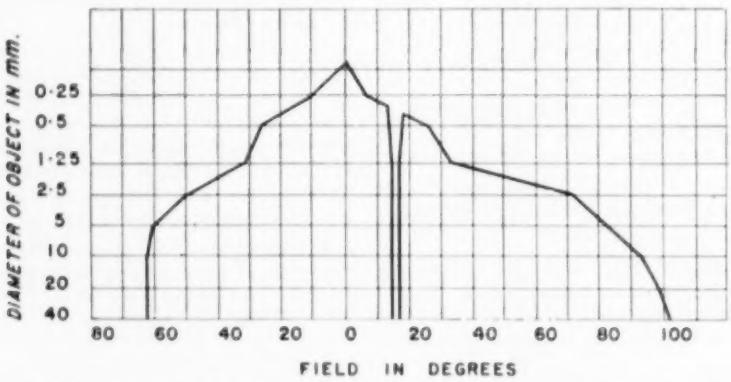


Fig. 1.—Plot of degrees of field from the fixation point for different-sized test objects. After Roenne, H.: Arch. Augenh. **78**:284, 1915; published by C. Hess, Weisbaden.

The work was done in a large room—about 25 ft. wide, 50 ft. long, and 15 ft. high. The walls were painted black. At one end of the room was a large, mat-white screen fastened to the wall. The screen was about 10 ft. high and 15 ft. across and had a reflectance of 80.8%. The fixation object at the center of the screen was a thumb tack 1 cm. across, painted white, with a black cross at its center joining a black circle at its outer edge. Intervals of 10 cm. were marked from the center to the periphery of the screen, by small pencil marks. The examiner wore a white coat. The subject sat facing the screen with his back to the room, on a platform so raised that his eye was level with the center of the screen. A chin rest was not used; however, the subject's head was held in a rest coming from the back of the chair. The test objects were made from Munsell neutral papers, ranging from No. 5 to No. 9 values. These were cut into round, flat objects, varying from 2 to 10 mm. in diameter, and mounted on fine, white rods. The lighting was obtained from diffuse reflectors set on either side of the subject. The number and the power of the lamps which were used varied according to the illumination which was desired. The color temperature of the lamps was not the same for all levels of illumination. Sixty-watt tungsten lamps were used at 6 ft-c.; 150-watt lamps, at 20 ft-c., and Photoflood bulbs, at the high illuminations. The lights of the room were turned out.

The illumination on the screen was tested with a Macbeth illuminometer, and the findings were checked with a photometer (Model 520 M of the Photovolt Corporation). With the Macbeth instrument, for each illumination, readings at seven positions on the screen—straight ahead, right, left, upper right, lower right, upper left, lower left—were done. The lamps were arranged so that the illumination did not vary more than 20% across the screen. The illuminations used were 6, 20, 110, 225, 525 and 825 ft-c.

The reflectances supplied by the Munsell Corporation for their papers were accepted. The reflectance of the tangent screen was tested with the illuminometer, against both the standard supplied with the instrument and the given reflectance of a Munsell paper. There was a close check between the figures obtained using the two standards. Table 1 gives the reflectance of the screen, the reflectances of the test objects, and the contrast between the screen and the test objects. The contrasts were calculated according to the formula $Co = \frac{Bt-Bo}{Bo}$, where *Co* stands for inherent contrast; *Bt*, brightness of target, and *Bo*, brightness of background.

Technique of Testing.—A shield with a pad was placed over one eye of the subject. He sat in the chair with his head against the rest, looking at the fixation object at the center of the screen. The examiner moved the test object in from the side of the screen at an approximately constant rate of 10 cm. per second, without jiggling the test object. When the subject first saw the object he said "yes." The examiner read the distance from the screen, and the subject wrote the reading on a piece of paper on his lap. The findings in 12 meridians were recorded, that is, at every 30 degrees.

TABLE 1.—*Reflectances of Screen and Test Object, with Contrast Calculated by Formula*

Reflectance of Screen	Reflectance of Object	Contrast
80.8%	16.7%	−0.79
	29.6%	−0.63
	44.2%	−0.45
	53.1%	−0.34
	73.0%	−0.097

A limited number of subjects were used, 10 in all. All the subjects had 20/20, or 20/30, visual acuity in either eye. All the subjects did not work at all levels of illumination, although most of them worked at several levels. Each had one or more practice sessions. The duration of the sessions was limited to 30 minutes because after longer periods the subject became tired and the results wandered.

Five subjects were used at each illumination, except at the highest and at the lowest illumination, where three subjects were used. At the levels of illumination at which a subject worked, he completed one reading for all the sizes of test objects, for all the brightnesses of test objects, and for all the meridians.

The standard working distance was 2000 mm.; however, it was found that when test objects smaller than 2 mm. were used the rod could be a guide to the test object. Therefore, the smaller-sized objects were replaced by larger objects and working distances up to 10,000 mm.

RESULTS

The radii of the visual fields were averaged for each size, for each contrast, and for each illumination. When working distances greater than 2000 mm. were used, the radii of the visual fields were reduced to correspond to the shorter working distance. Table 2 gives the radii of the visual fields, in centimeters, for a working distance of 2000 mm., for each size of test object, and for each contrast.

ANALYSIS

To rearrange the data, we assumed that the 10 mm. test object is our standard-sized object seen at 2000 mm. and that the smaller-

TABLE 2.—*Radii of Visual Fields, in Centimeters, for Each Size Test Object, Contrast, and Illumination*

Illumination	Diameter of Object, Mm.	C* = −0.79	C = −0.63	C = −0.45	C = −0.34	C = −0.097
6 ft-c	10	118 cm.	110 cm.	99 cm.	90 cm.	53 cm.
	9	...	...	...	...	..
	8	106	97	88	76	45
	7	...	...	...	...	..
	6	89	81	75	55	26
	5	...	...	...	...	..
	4	66	65	62	40	28
	3	45	41	36	22	16
	2	33	29	28	11	12
	1	14	10	9	6	4
	4/5	6.4	4.4	3.6	2.2	1
	3/5	4.8	3.0	1.8	1.2	..
	2/5	0.6	0.4	0.2	...	..
20 ft-c	10	128	120	115	106	73
	9	123	117	111	97	65
	8	118	111	104	93	63
	7	113	104	99	88	58
	6	101	95	96	84	51
	5	92	89	86	76	47
	4	85	81	81	66	42
	3	51	51	45	39	23
	2	38	39	36	30	19
	1	18	15	16	12	9
	4/5	5.4	5.2	4.4	2.6	0.6
	3/5	3.8	3.0	2.0	0.8	..
	2/5	1.6	0.8	...	...	..
110 ft-c	10	128	123	114	93	65
	9	127	118	104	86	53
	8	124	112	98	81	52
	7	113	105	92	78	49
	6	108	100	90	71	41
	5	98	93	82	62	34
	4	84	82	76	55	34
	3	54	54	49	36	20
	2	41	41	37	26	16
	1	20	15	17	12	8
	4/5	8.8	7.6	6.8	4	0.8
	3/5	6.8	5.4	4.6	2.4	0.4
	2/5	1.2	1.1	0.8	0.4	0.2
225 ft-c	10	128	126	121	107	70
	9	...	...	...	...	..
	8	120	117	107	94	59
	7	...	...	...	...	..
	6	101	98	90	71	43
	5	...	...	...	...	..
	4	85	80	77	53	33
	3	58	51	46	32	20
	2	41	39	33	20	14
	1	16	11	11	9	6
	4/5	6.6	3.6	3.4	2.6	1.2
	3/5	3.2	2.6	2.2	1.8	0.6
	2/5	1	0.8	0.8	0.6	0.1
525 ft-c	10	135	129	121	112	80
	9	...	...	...	...	..
	8	125	121	111	102	69
	7	...	...	...	...	..
	6	109	106	97	81	50
	5	...	...	...	...	..
	4	92	82	86	67	49
	3	61	58	55	43	25
	2	45	43	45	32	18
	1	20	16	15	12	8
	4/5	10	7.6	6.6	4.2	2.6
	3/5	7.4	5.6	4.0	3.6	0.8
	2/5	1.4	1.0	0.8	0.8	0.4
822 ft-c	10	130	128	122	103	79
	9	...	...	...	...	..
	8	125	118	112	91	74
	7	...	...	...	...	..
	6	115	106	98	76	55
	5	...	...	...	...	..
	4	98	87	86	67	51
	3	59	58	55	42	26
	2	48	42	47	32	20
	1	21	14	15	10	8
	4/5	10	7.4	6.4	3.6	1.6
	3/5	8	5.4	4.4	2.8	0.4
	2/5	2.2	1.0	0.8	0.4	..

* C = contrast.

TABLE 3.—*Visual Field Radii, in Millimeters, for Standard Test Object Viewed at Distances Starting from 2000 Mm.*

Illumination	Position in Space, Mm.	C* = −0.79	C = −0.63	C = −0.45	C = −0.34	C = −0.097
6 ft-c	2,000	1180 mm.	1100 mm.	980 mm.	900 mm.	530 mm.
	2,222	....	....	....	....	....
	2,500	1320	1208	1096	955	561
	2,857	....	....	....	....	....
	3,333	1473	1347	1248	916	560
	4,000	....	....	....	....	....
	5,000	1650	1625	1550	1000	700
	6,666	1497	1364	1198	732	533
	10,000	1650	1450	1400	550	600
	20,000	1400	1000	800	600	400
	25,000	800	560	450	276	126
	33,000	800	500	300	200	....
	50,000	150	100	50	....	....
20 ft-c	2,000	1280	1200	1150	1000	730
	2,222	1364	1297	1231	1076	721
	2,500	1470	1383	1412	1158	785
	2,857	1613	1483	1412	1256	827
	3,333	1680	1581	1597	1397	848
	4,000	1838	1706	1740	1520	939
	5,000	2126	2026	2026	1650	1060
	6,666	1697	1697	1497	1297	765
	10,000	1900	1850	1800	1500	960
	20,000	1800	1500	1600	1200	900
	25,000	676	650	550	325	76
	33,000	634	500	334	134	....
	50,000	40	20	....	....	....
110 ft-c	2,000	1280	1220	1140	930	650
	2,222	1408	1309	1154	932	588
	2,500	1544	1365	1221	1010	647
	2,857	1613	1499	1313	1114	699
	3,333	1706	1693	1497	1181	682
	4,000	1879	1859	1636	1240	680
	5,000	2100	2050	1900	1375	850
	6,666	1790	1796	1630	1198	665
	10,000	2050	2050	1850	1300	800
	20,000	2000	1500	1700	1200	800
	25,000	1100	950	850	500	100
	33,000	1133	800	700	400	66
	50,000	300	275	200	100	50
225 ft-c	2,000	1280	1200	1210	1070	700
	2,222	....	....	....	....	....
	2,500	1494	1457	1393	1170	740
	2,587	....	....	....	....	....
	3,333	1680	1630	1497	1181	715
	4,000	....	....	....	....	....
	5,000	2125	2000	1925	1325	825
	6,666	1784	1697	1631	1065	665
	10,000	2050	1900	1650	1082	700
	20,000	1600	1100	1100	800	600
	25,000	825	450	425	325	150
	33,000	500	433	300	300	100
	50,000	250	200	200	150	25
525 ft-c	2,000	1350	1290	1210	1120	800
	2,222	....	....	....	....	....
	2,500	1557	1507	1393	1270	850
	2,587	....	....	....	....	....
	3,333	1814	1764	1614	1347	682
	4,000	....	....	....	....	....
	5,000	2300	2051	2150	1675	1225
	6,666	2030	1930	1830	1431	832
	10,000	2250	2150	2250	1600	900
	20,000	2000	1600	1500	1200	800
	25,000	1250	950	734	525	325
	33,000	1233	933	575	600	134
	50,000	350	250	200	200	100
822 ft-c	2,000	1360	1280	1220	1080	790
	2,222	....	....	....	....	....
	2,500	1557	1470	1393	1134	922
	2,587	....	....	....	....	....
	3,333	1914	1764	1630	1265	915
	4,000	....	....	....	....	....
	5,000	2325	2175	2150	1657	1276
	6,666	1963	1930	1830	1297	895
	10,000	2400	2100	2250	1600	1000
	20,000	2100	1400	1500	1000	800
	25,000	1275	925	800	450	200
	33,000	1333	866	733	466	66
	50,000	550	250	200	100	....

* C = contrast.

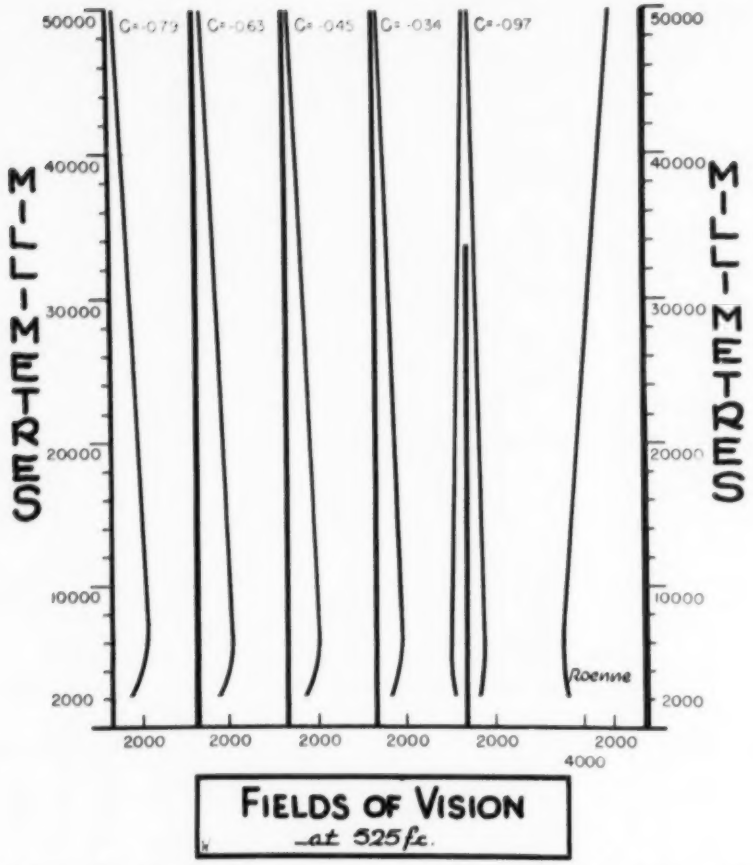


Fig. 2.—Limits of the visual field for a 10 mm. round test object, under different conditions of contrast and 525 ft-c. of illumination.

sized objects merely represent a 10 mm. object seen at a greater distance; that is, a 5 mm. object would be equivalent to a 10 mm. object seen at 4000 mm., a 2 mm. object would be equivalent to a 10 mm. object seen at 10,000 mm., and a 0.4 mm. test object would be equivalent to a 10 mm. object seen at 50,000 mm. For each of these longer viewing distances the radii of the visual fields are correspondingly increased; for example, for a viewing distance of 4000 mm. the radii are doubled. We have followed Glees and Fröhlich [2] (1950), who found that visual fields taken at different working distances are comparable. Table 3 shows all the figures converted to a standard test object, 10 mm. diameter, viewed at distances starting from 2000 mm. The subsequent graph (Fig. 2) presents a sample from these figures, drawn to scale, with data from Roenne [1] added.

In considering the visual limits for an unknown object, the brightness of the background and the brightness of the surface of the object must be known; the contrast between background and object can be calculated. For great working distances the contrast must be corrected for attenuation of contrast by the atmosphere. After making these adjustments, for contrast and for attenuation of contrast, the figures in Table 3 can be used to calculate the limits of vision during a single glance.

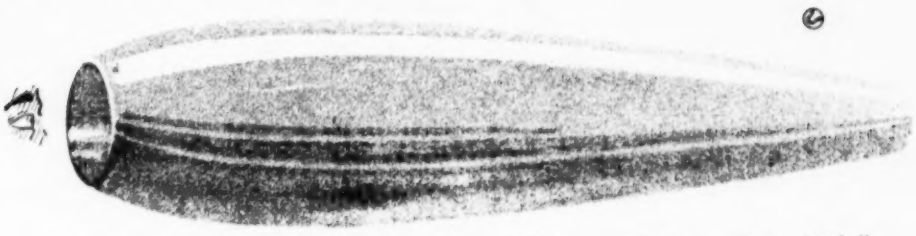


Fig. 3.—Diagrammatic presentation of the visual field for a round object, such as a baseball.

The analysis is made on the basis of a round object 10 mm. in diameter, or having an area of 78.5 sq. mm. To develop figures for any unknown object, we can follow the procedure of calculating areas of Lamar, Hecht, Shlaer, and Hendley [3] (1947). For any chosen aspect of the object, the total angular subtense, in terms of visible area, is found. If the length of the object is less than 10 times the width, the shape can be disregarded; the object is assumed to be round, having the area already discovered. The diameter of such a round figure is calculated, and this diameter is divided by 10, the diameter of the 10 mm. object. Both the distances and the sizes of field in Table 3 are multiplied by this factor, to give the size of field, for various distances from the observer, of the chosen object.

COMMENT

These limits of vision for any one instant do not look like the visual fields seen in the textbooks. When portrayed as different-sized objects at a constant working distance, the limits of vision make a mushroom-shaped figure (Fig. 1). However, when depicted as a constant object seen at varying distances, the limits of vision become a needle-like figure reaching far out into space (Fig. 3). This last presentation is more in keeping with reality, where we commonly see an object of a given size at various distances.

SUMMARY

The fields of vision of dark objects on a white background have been mapped for different sizes of test objects, different contrasts between object and background, and different quantities of illumination. These data have been calculated, assuming a constant-sized object seen at different working distances. The fields so obtained are long, needle-like figures, whose forms indicate the low probability of seeing a small object in the distance and the true shape of visual space about us.

REFERENCES

1. Roenne, H.: Zur Theorie und Technik der Bjerrumschen Gesichtsfelduntersuchung, Arch. Augenh. **78**:284, 1915.

2. Glees, M., and Fröhlich, G.: Über die Bedeutung des Aubert-Förstercheu Phänomens fur die Gesichtsfeldprufung, von Graefes Arch. Ohpth. **151**:195, 1950.

3. Lamar, E. S.; Hecht, S.; Shlaer, S., and Hendley, C. D.: Size, Shape and Contrast in Detection of Targets by Daylight Vision: I. Data and Analytical Description, J. Optic. Soc. America **37**: 531, 1947.

Intravenous Treatment of Optic Neuritis

Comparison of Corticotropin and Typhoid Bacilli

PHILIP KAZDAN, M.D.
and
ROSCOE J. KENNEDY, M.D., Cleveland

There are many reports in the current literature on the intravenous use of corticotropin and of typhoid; however, there are no articles comparing their clinical use in ophthalmology. This study was undertaken in order to ascertain the clinical value of intravenous corticotropin (ACTH; adrenocorticotropic hormone) in comparison with that of intravenous killed typhoid bacilli in the treatment of optic neuritis: We have compared the results of treatment in two groups of patients, one in which the treatment was with corticotropin and the other in which it was with killed typhoid bacilli.

It has been shown by Olson and associates[1] that nonspecific foreign protein, i. e., killed typhoid organisms, among other drugs, produces changes in the adrenal cortex which are characteristic of the general response to stress, and that the benefit derived from this form of therapy could be attributed to the release of endogenous adrenocorticotropic hormone.* The same type of changes can be produced by the injection of corticotropin.

There are several reports confirming the beneficial results obtained with corticotropin in the treatment of acute inflammatory lesions of the eye.† In treating inflammation of the posterior ocular segment, the method of administration of corticotropin is important. Favorable results were obtained by Woods[6] only in those cases treated parenterally. Topical applications of the drug, either as ointment or as orbital injections of corticotropin, were not effective. Woods also pointed out that when the optic neuritis was secondary to a demyelinating process, it was difficult to decide whether the apparent improvement was a natural remission or the result of therapy. Smith[7] reported the use of intravenous corticotropin in two cases of optic neuritis, with improvement in one case. He used doses of 10 to 40 mg. of corticotropin in 1000 cc. of 5% dextrose in water with slow drip, lasting six to eight hours. Treatment was continued for 10 days, followed by a tapering-off dose of 25 mg. of cortisone given orally four times a day for one week. This dosage schedule was determined by the work of McIntosh and Holmes,[8] who recommend a dose of 10 to 20 mg. of corticotropin daily given intravenously.

METHOD OF STUDY

Every patient was examined by a consulting neurologist. Those patients who in the neurologist's opinion had optic neuritis secondary to a demyelinating process were excluded from this study; 22 patients qualified. All the patients were hospitalized and received complete physical and neurologic examinations. Each patient was placed on a low-salt diet, 0.2% potassium chloride being added to the intravenous solution. The blood pressure, weight, urinalysis, and eosinophile count were recorded daily.

The first group of patients included 11 alternate patients who were given 20 mg. of corticotropin in 500 cc. of 5% dextrose in distilled water intravenously by slow drip, lasting six to eight hours. After 10 daily doses of 20 mg. of corticotropin, the dose was tapered off to 25 mg. of oral cortisone four times a day for two weeks.

The second group of patients included 11 in whom intravenous typhoid therapy was started with an initial dose of 25,000,000 KTB. Subsequent doses were given after a 24-hour afebrile period. The dose was doubled with each injection until a total injection containing 400,000,000 KTB was given.

For the sake of uniformity in this study, all factors other than treatment, such as diet, weight recording, blood tests, and vitamin administration, were identical in the two groups.

From the Department of Ophthalmology, The Cleveland Clinic Foundation, and The Frank E. Bunts Educational Institute.

* References 1 and 2.

† References 3, 4, and 5.

RESULTS

The results are summarized in the Table. There was no case of bilateral optic neuritis in the group treated with corticotropin; however, there were two such cases in the group treated with intravenous typhoid bacilli. One patient treated with corticotropin had a relapse five weeks after the last treatment. He was given a second course of 10 daily doses of intravenous corticotropin, followed by a tapering off with 25 mg. of oral cortisone four times a day for two weeks. A 13-month follow-up after the second course of treatment has revealed no recurrence. This

Comparison of Two Groups of Patients with Optic Neuritis

Factors	Treated with Intravenous Killed Typhoid Bacilli	Treated with Intravenous Corticotropin
Age, yr.	Range 20-67 Average 48.7	Range 14-73 Average 50.6
Sex	F 7 M 4	F 4 M 7 *
Duration of symptoms	Range 3 days-2 mo. Average 12 days	Range 2 days-3 mo. Average 16 days
No. of eyes treated	13 †	12 *
Visual acuity	Improved 6 Decreased 3 Unchanged 4	Improved 6 Decreased 3 Unchanged 3
Fields	Improved 7 Decreased 1 Unchanged 5	Improved 8 Decreased 0 Unchanged 4
Follow-up	Range 10 mo.-2 yr. Average 11.8 mo.	Range 7 mo.-2 yr. Average 10.5 mo.

* One patient given second course of corticotropin because of relapse.
† Two patients had bilateral optic neuritis.

is strong evidence, as reported by McLean, Gordon, and Koteen,[9] of a drug-induced result.

Comparison of the 25 eyes treated, 12 with corticotropin and 13 with typhoid bacilli, shows a marked parallelism in the results obtained by these two methods. Comparisons of visual acuity and fields were made, the first being done at the time of the original diagnosis and the latter at the last follow-up visit. Field examination included both perimetry and tangent screen studies. As pointed out by Smith,[7] subjective improvement was greatest on the third day of intravenous use of corticotropin. Final results of this method of treatment could almost be predicted on this third day of treatment. No such dramatic recovery was observed in any case successfully treated with intravenous typhoid bacilli. During active treatment, patients in the two groups complained equally, one from the reaction of chills and fever induced by the intravenous killed typhoid bacilli; the other from enforced inactivity necessitated by the 6- to 8-hour drip.

CONCLUSION

Two groups of patients with optic neuritis who at the time of treatment were not thought to have a demyelinating disease were treated. One group of 11 patients was treated with intravenous killed typhoid bacilli, and the other group of 11 patients, with intravenous corticotropin. Comparison of the results obtained from these two methods of treatment shows no superiority of one method over the other, especially as regards visual acuity.

REFERENCES

1. Olson, J. A.; Steffensen, E. H.; Margulis, R. R.; Smith, R. W., and Whitney, E. L.: Effect of ACTH on Certain Inflammatory Diseases of the Eye: A Preliminary Report, J. A. M. A. **142**:1276-1278 (April 22) 1950.

2. Sayers, G., and Sayers, M. A.: The Pituitary-Adrenal System, Ann. New York Acad. Sc. **50**: 552-539, 1949.

3. Olson, J. A.; Steffensen, E. H.; Smith, R. W.; Margulis, R. R., and Whitney, E. L.: Use of Adrenocorticotropic Hormone and Cortisone in Ocular Disease, A. M. A. Arch. Ophth. **45**:274-300 (March) 1951.

4. Gordon, D. M., and McLean, J. M.: Effects of Pituitary Adrenocorticotropic Hormone (ACTH) Therapy in Ophthalmologic Conditions, J. A. M. A. **142**:1271-1276 (April 22) 1950.

5. Fitzgerald, J. R., and others: Early Clinical Results of ACTH and Cortisone Treatment of Ocular Disease, A. M. A. Arch. Ophth. **45**:320-333 (March) 1951.

6. Woods, A. C.: Present Status of ACTH and Cortisone in Clinical Ophthalmology, Am. J. Ophth. **34**:945-960 (July) 1951.

7. Smith, E. L.: Intravenous Use of Corticotropin in Optic Neuritis, A. M. A. Arch. Ophth. **49**:303-312 (March) 1953.

8. McIntosh, H. W., and Holmes, C. B.: Intravenous Use of ACTH, Canada. M. A. J. **65**:33-35 (July) 1951.

9. McLean, J. M.; Gordon, D. M., and Koteen, H.: Clinical Experiences with ACTH and Cortisone in Ocular Diseases, Tr. Am. Acad. Ophth. **55**:565-572 (May-June) 1951.

A Simple Nomogram for Problems in Optics

S. I. ASKOVITZ, M.D., Philadelphia

The practitioner, while reviewing the basic principles of geometric optics essential for a proper understanding of ophthalmic refraction, often finds himself handicapped by lengthy decimal calculations. The fundamental properties of spherical lenses and mirrors are frequently lost in jumbles of compound fractions and long division.*

As an aid to physicians studying to become oculists, the following nomogram was devised to help eliminate the arithmetical drudgery of verifying optical bench experiments and to assist in visualizing the basic object-image relationships. The nomogram is easy to draw accurately, requiring only ruler and compass, or protractor.

THE NOMOGRAM

Draw three straight lines passing through a common point, one vertical and the other two making angles of 60 degrees with the first (and with each other). Place arrows at the upper ends of the lines, and indicate, from left to right, p for object distance, f for principal focal distance, and q for image distance,† as shown (Fig. 1). Mark off equal units along the three axes, according to any convenient scale. Positive distances are represented in the direction of the arrows, and negative distances, in the opposite sense.

APPLICATION

Positive distances refer to real objects (in front of the lens or mirror, with divergent pencils of incident light rays), real images (behind the lens or in front of the mirror), and principal focal lengths of converging optical systems (convex lens or concave mirror, with real focal point). Negative distances refer to virtual objects (convergent pencils of incident light rays, directed toward a point behind the lens or mirror), virtual images (i. e., pencils of light rays appearing to diverge from a point in front of the lens or behind the mirror), and principal focal lengths of diverging optical systems (concave lens or convex mirror, with virtual focal point). The advantage of this type of sign convention ‡ is that it permits the use of a single formula (the Gaussian equation $1/p + 1/q = 1/f$) for both lenses and mirrors. (Paraxial rays correspond to lines parallel to the p or q axes, when object or image is "at infinity.")

In applying the nomogram to numerical problems, it is assumed that two of the

NOMOGRAM FOR PROBLEMS IN OPTICS

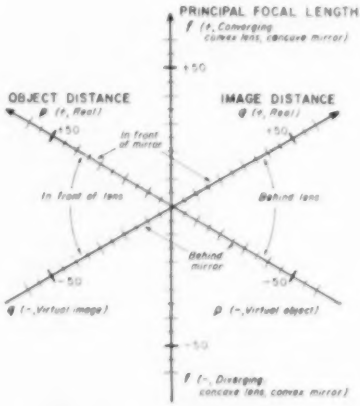


Fig. 1.—Nomogram representing the equation $1/p+1/q=1/f$.

The nomogram has been satisfactorily applied by student-physicians at the Graduate School of Medicine of the University of Pennsylvania for the past three years.

From the Ophthalmology Research Laboratory (Dr. I. H. Leopold, Director), Albert Einstein Medical Center, Northern Division. This work was made possible by a research grant from the Weinstock Fund.

* Boeder, P., cited in Reference 1, p. 513.

† Pascal,[2] p. 752.

‡ Pascal,[2] pp. 457-459.

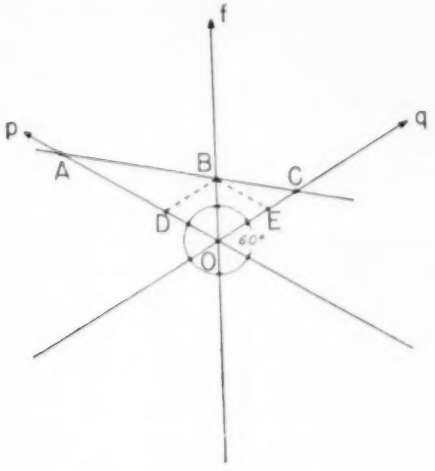


Fig. 2.—Proof of the nomogram.

three distances f, p, and q have been measured or are known. The two given values are noted on their respective axes, and a ruler, card, or other straightedge is placed through the two points. The point at which the straightedge crosses the third axis is noted. This automatically provides the unknown value, with its correct plus or minus sign.

When the p and q distances are represented on the same side of the f axis (both to the right or both to the left), then the image is erect; if on opposite sides, the image is inverted.

Furthermore, the magnification ratio may be seen at a glance by comparing the lengths of p and q, since the ratio of image size to object size is as image distance is to object distance ($I : O = q : p$).

PROOF

The fundamental validity of the nomogram follows directly from the proportionality of corresponding parts of similar triangles (Fig. 2). Let A, B, and C be any set of collinear points on the p, f, and q axes, respectively, and let O represent the central point of the nomogram. Draw BD parallel to CO and BE parallel to AO. Then, since the angles are all equal to 60 degrees, the triangles BDO and BEO are each equilateral, so that $OD = DB = OB = OE = EB$.

Then

$$\frac{1}{p} + \frac{1}{q} = \frac{1}{OA} + \frac{1}{OC} = \left(\frac{OB}{OA} + \frac{OB}{OC}\right) \cdot \frac{1}{OB} =$$

$$\left(\frac{EB}{OA} + \frac{DB}{OC}\right) \cdot \frac{1}{OB} = \left(\frac{BC}{AC} + \frac{AB}{AC}\right) \cdot \frac{1}{OB} = \frac{AC}{AC} \cdot \frac{1}{OB} = \frac{1}{f}$$

Thus, the algebraic equivalent of the nomogram is precisely the basic Gaussian equation.

NUMERICAL EXAMPLES

1. Assume that a given spherical lens produces a sharp image of an object placed 30 cm. in front of the lens, at a distance of 60 cm. behind the lens (Fig. 3). What is the principal focal length of this lens, and what is the object-image relationship?

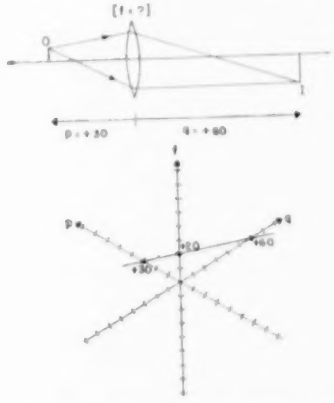


Fig. 3.—Application of the nomogram: object and image distances given.

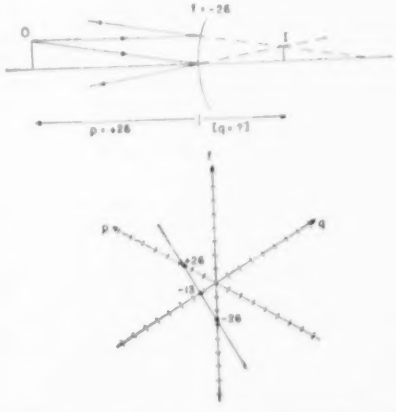


Fig. 4.—Application of the nomogram: object distance and focal length given.

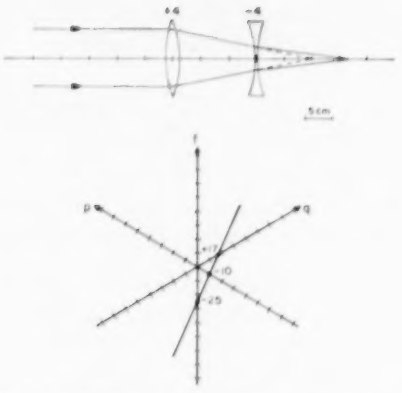


Fig. 5.—Application of the nomogram: virtual object.

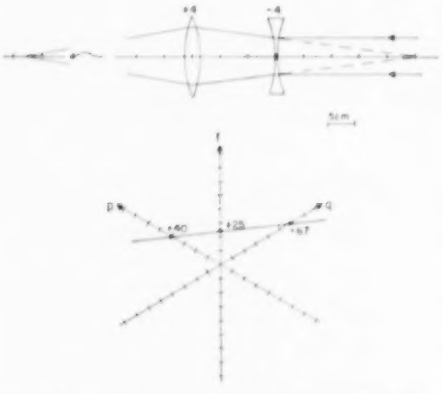


Fig. 6.—Application of the nomogram: incident rays from the right.

Solution.—Mark +30 on the object-axis and +60 on the image-axis. A ruler is placed with its edge through these two points. The resulting line crosses the *f*-axis at a point representing +20. Therefore, the lens is convex and has a principal focal length of 20 cm. The image is inverted (on the opposite side of the *f*-axis) and enlarged. The exact magnification ratio equals $q:p=60:30=2:1$.

2. An object is placed 26 in. in front of a convex mirror having a principal focal length of 26 in. (Fig. 4). Where is the image?

Solution.—The points marked on the axes are $p=+26$ and $f=-26$. The result is immediately read on the nomogram, $q=-13$. This represents an erect virtual image 13 in. behind the mirror (with magnification ratio of 1:2).

3. Given an optical system consisting of a +4 D. spherical lens placed 15 cm. to the left of a −4 D. spherical lens, what is the outcome of paraxial rays of light striking the combination of lenses (*a*) from the left and (*b*) from the right?

Solution.—(*a*) (Fig. 5) The convex lens causes parallel rays from the left to converge toward a point on the principal axis 25 cm. to the right of this lens. These converging rays of light, striking the concave lens, are equivalent to a virtual object 10 cm. behind the lens. Applying the nomogram to $p=-10$ and $f=-25$, the result is $q=+17$, approximately. This implies that the right-hand principal focal point for the system is about 32 cm. from the convex lens.

(*b*) (Fig. 6) Starting with parallel rays of light approaching the optical system from the right, the concave lens will cause them to diverge as though coming from a point 25 cm. to the right of the lens. These divergent rays then strike the convex lens, with an object distance equivalent to +40 cm. (plus because the light rays are divergent as they strike the lens; that they come from the right does not matter). The effect of the lens is estimated immediately on the nomogram, taking $p=+40$ and $f=+25$. The value found for q is seen to be about +67. Therefore, the left-hand principal focal point of the system is 67 cm. to the left of the convex lens.

OBJECT-IMAGE RELATIONSHIPS

The nomogram may be applied to study the general relationship between object and image points for spherical lenses or mirrors, either convex or concave. It may simplify the graphic visualization to place the lens at the center of the diagram, with its principal axis horizontal. Figure 7 shows the various possibilities for conjugate focal points in the case of a convex lens.[3]

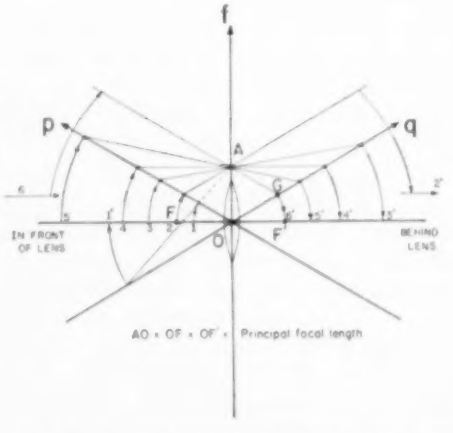


Fig. 7.—General object-image relationship for a convex spherical lens.

1. If the object is closer to the lens than the principal focal point, there will result a virtual, enlarged, erect image. This illustrates the use of such a lens as a magnifying glass.

2. An illuminated object placed at the principal focal point will result in emergent rays parallel to the principal axis.

3. With object beyond the focal point, but less than twice this distance from the lens, the image will be enlarged, real, and inverted.

4. In the special case in which the object distance is exactly twice the principal focal length, the "nomogram" line will be horizontal, and the image will have the same size as the object.

5. For an object anywhere on the principal axis more than twice the principal focal length from the lens, the image will be real, inverted, and reduced in size.

6. In the case of an object at "infinity," or in the instance of parallel incident rays, the straightedge is to be placed parallel to the p-axis and drawn through the point A (as are all the lines for this particular lens). This line crosses the q-axis at a point G, which may be projected down to the corresponding point F'. Because the triangles are all equilateral, it is easily seen that this represents the principal focal point behind the lens.

A similar analysis is readily made for concave lenses or for convex or concave spherical mirrors.

SUMMARY

A simple nomogram is presented for the graphic solution of numerical problems dealing with spherical lenses and mirrors. With burdensome calculations eliminated, the student of optics may concentrate his attention upon basic principles rather than arithmetical details. The nomogram also provides a convenient review of the fundamental object-image relationships.

REFERENCES

1. Ruedemann, A. D., Chairman: Teachers Section in Ophthalmology, Tr. Am. Acad. Ophth. **58:** 508-519 (May-June) 1954.

2. Pascal, J. I.: Studies in Visual Optics, St. Louis, C. V. Mosby Company, 1952.

3. Duke-Elder, W. S.: Text-Book of Ophthalmology, Vol. I, St. Louis, C. V. Mosby Company, 1938, p. 702.

Incidence of Coagulase-Positive Staphylococci in External Ocular Infections

TED SUIE, Ph.D.
and
FRANK W. TAYLOR, M.D., Columbus, Ohio

The surveys concerning the microflora of external ocular infections in the United States generally indicate that staphylococci are the commonest bacteria encountered.* Therefore, the need commonly arises (for obvious epidemiologic, bacteriologic, and clinical reasons) to differentiate the pathogenic from the nonpathogenic strains. In the past such criteria as hemolysis on blood plates, fermentation of mannitol, pigmentation, and liquefaction of gelatin have been employed. However, it is generally agreed that these characteristics can only serve as presumptive evidence of pathogenicity, since the nonpathogenic strains may also exhibit similar reactions, usually to a slighter degree. Furthermore, the pathogenic strains may vary considerably in their biochemical reactions as well as in the production of pigment.

The ability of certain staphylococci to coagulate citrated or oxalated plasma was first described in 1903 by Loeb.[4] Cruickshank [5] and Thygeson,[6] as well as others, maintain that the coagulase test is the most reliable and convenient in vitro test for determining the pathogenicity of these organisms. Consequently, this test has become a widely accepted bacteriologic procedure in ophthalmic laboratories. Thus, the aforementioned cultural characteristics should be considered only supporting evidence of the pathogenic potentials of these bacteria. Smith and Hale [7] have conducted investigations to determine the nature and mode of action of staphylocoagulase. They state that coagulase is a thermostable substance which acts as a precursor of a thrombin-like substance.

This present investigation was undertaken to ascertain whether a greater percentage of coagulase-positive staphylococci do occur in external ocular infections than in normal eyes.

METHODS AND MATERIALS

Two groups of subjects were selected: the first with primary conjunctivitis and the second with no evidence of external ocular infection. All cultures were obtained from the lower cul-de-sac with strict aseptic technique and subsequently treated in the same manner. This report includes only those subjects from whom staphylococci were recovered.

The staphylococci were isolated on blood plates, and 24-hour cultures of these organisms were emulsified in brain-heart infusion broth. One-half milliliter of commercially prepared plasma solution † was placed in a Wassermann tube and 2 drops of the emulsified culture was added. The tubes were incubated at 37 C for one hour and the first reading made. If necessary, the tubes were again incubated for two hours and a second reading made. Absence of clotting after 24 hours of incubation was considered a negative reaction. Any degree of clotting was regarded as a positive reaction. The hemolytic activity of the organisms was determined on rabbit blood-brain-heart infusion plates.

Seena G. Lewine and Ruth Duncan gave technical assistance.

The statistical analyses were made through the cooperation of the Statistics Laboratory, Mathematics Department, the Ohio State University.

* References 1 through 3.

† Bacto Coagulase Plasma, Difco Laboratories, Inc., Detroit.

FINDINGS

The Table shows the incidence of coagulase-positive staphylococci in patients with external ocular infections, as compared with persons who demonstrated no clinical manifestations of such infections. Coagulase-positive staphylococci were isolated from 51% of the patients, as compared with 10% in the normal group. As may be noted (Table), the percentage of hemolytic strains was strikingly similar in the two groups. The following analysis was reported by the Ohio State University Statistics Laboratory, to which these data were submitted for revaluation of significance:

One hundred and eighteen individuals have been classified according to two separate criteria into one of two levels. The resulting arrangement is called a contingency table. The hypothesis to be tested is whether the two criteria for classification are independent. The statistic

$$\chi^2=\sum_{i=1}^{k}\frac{(o_i-e_i)^2}{e_i}$$

is used to test the hypothesis. A large value of χ^2 is inconsistent with independence of the two criteria of classification. The contingency table and the necessary computations for χ^2 are presented in the Table. The computed $\chi^2=19.220$ may be considered large, or significant, because the probability of obtaining as large a χ^2 is less than 1% if the hypothesis is correct.

Incidence of Coagulase-Positive Staphylococci in Patients with External Ocular Infections as Compared with That in Patients with No Clinical Evidence of External Ocular Infections

	No. of Cases from Which Staphylococci Were Isolated	No. of Coagulase-Positive	%	No. of Coagulase-Negative	%	No. of Hemolytic Strains	%	No. of Nonhemolytic Strains	%
Patients with primary conjunctivitis..	78	40 (29.1)*	51	38 (48.9)	49	63	81	15	19
Persons with no external ocular infections	40	4 (14.9)	10	36 (25.1)	90	33	82	7	18

* Figures in brackets are the expected values for χ^2.

COMMENT

This study has demonstrated a statistically significant increase in the percentage of coagulase-producing organisms isolated from cases of external ocular infections as compared with those from normal eyes. Supported by these findings, we believe the coagulase test is a reliable in vitro criterion of the potential pathogenicity of the staphylococci. It is our practice to use this test routinely in our bacteriologic studies.

SUMMARY AND CONCLUSIONS

Staphylococci were isolated from 40 normal eyes and 78 eyes with conjunctivitis.

A significantly greater percentage of strains from diseased eyes (51%) were coagulase-positive as compared with strains from normal eyes (10%).

The coagulase test is a desirable aid in the evaluation of potential pathogenicity of the staphylococci.

Department of Ophthalmology, Ohio State University.

REFERENCES

1. Soudakoff, P. S.: Bacteriologic Examination of the Conjunctiva, Am. J. Ophth. **38**:374, 1954.

2. Thygeson, P.: Bacteriologic Differentiation of the Common Forms of Conjunctivitis with Particular Reference to Types Prevailing in Iowa, J. Iowa M. Soc. **27**:15, 1937.

3. Suie, T.: Microflora of Conjunctivitides with Special Reference to Types Prevailing in Central Ohio, Ohio State M. J., to be published.

4. Loeb, L.: Influence of Certain Bacteria on the Coagulation of Blood, J. M. Res. **10**:407, 1903-1904.

5. Cruickshank, R. J.: Staphylocoagulase, J. Path. & Bact. **45**:295, 1937.

6. Thygeson, P.: The Eye and Its Diseases, edited by Conrad Berens, Philadelphia, W. B. Saunders Company, 1949, p. 1039.

7. Smith, W., and Hale, J. H.: Nature and Mode of Action of Staphylococcus Coagulase, Brit. J. Exper. Path. **25**:101, 1944.

Late Effects of Beta Radiation on the Eye

GEORGE R. MERRIAM Jr., M.D., New York

The value of radiotherapy in ophthalmology has been known for many years. The history of its development and the original experimental and clinical work have been reviewed excellently by Desjardins.[1] During recent years there has been considerable enthusiasm for the use of beta radiation in the treatment of numerous ocular lesions.* Interest in this form of radiation has been furthered by the impression that it has no harmful effects. It is the purpose of this paper to call attention to the possible harmful sequelae and the approximate dosages that will produce these changes.

GENERAL RADIATION EFFECTS

Any radiation effect is produced only by the energy that is absorbed in the irradiated tissue. Rays that pass through the tissue without loss of energy produce no effect. The result is obtained, in essence, by the ionizing effect of the rays on the cell, especially on the nucleus, but also on the cytoplasm.

Beta rays, which are formed by the disintegration of a radioactive element, are really high-speed electrons with relatively low penetrability, and, as in all forms of radiation, they are ionizing radiations which are capable of producing changes in the tissues absorbing them. All radiation is destructive—never stimulating—no matter how small the dose.[11] There are three main types of radiation effects.[12]

1. Reversible effects, in which the changes are transient and end in complete restoration of the original function

2. Conditioned reversible effects, in which the changes induced by irradiation vanish completely but the restoration of normal function is only apparent, for further irradiation is not followed by a return to normal

3. Irreversible effects, in which therapy is not followed by a return to normal and the changes initiated continue to progress and persist for life

This classification is good in a general sense only, for the effects produced by a given amount of radiation will vary with many physical factors and the type of cells irradiated. In addition to a difference in tissue response, there is also an individual variation that is unpredictable.

Another important consideration is the fact that the late effects of therapy may take 5, 10, or 15 years to appear. In general, the time of onset is an inverse function of the dose—thus, the higher the dose the sooner the late effects may appear.

DOSAGE

The lack of uniformity of expressed dosage in beta therapy has led to considerable confusion. The terms millicurie-minute (mc-min.), gram-second (gm-sec.), and roentgen equivalent physical (rep) have all been employed. This makes it difficult, and at times impossible, to compare the results reported by different authors.

Since the unit of measure for x-rays and gamma rays is the roentgen (r), it is urged that the roentgen equivalent physical (rep) be adopted as the standard for beta radiation. Each applicator should be calibrated and the output in rep/sec. or rep/min. calculated. Not only will this result in better standardization of treatment, but it will enable the therapist to understand more fully the amount of treatment being administered. It

Dr. Edith Quimby gave technical advice.

This work was supported in part by a grant from the Snyder Ophthalmic Foundation.

From the Institute of Ophthalmology, Presbyterian Hospital, and the Memorial Center for the Treatment of Cancer and Allied Diseases.

* References 2 through 10.

will also allow a more accurate comparison of results from different institutions.

For the purpose of uniformity, all doses reported here have been transposed into roentgen equivalents physical (reps) unless otherwise stated, using the figures of Krohmer.[18] The rep here has been measured as 1 electrostatic unit of ionization per cubic centimeter of the air ionization chamber. Krohmer's work illustrates the extreme variability in output between even essentially similar applicators. His maximum variation from the mean for the applicators measured was —63%, with an average of approximately ±25%.

It is essential to appreciate that the output of each bulb must be calibrated individually under the exact conditions in which it will be used clinically. For instance, measurements by Focht † at the Memorial Center in New York on a few of their glass radon bulbs gave an output at the surface about three times Krohmer's value. However, the support of the Memorial Center applicator allowed a larger area of it to be exposed, and it was about 1 mm. closer to the surface than the Krohmer bulb. A small difference in the thickness of the glass will also make a large difference in the output. The per cent depth-dose curves of the two institutions agree fairly well.

The potential source of error inherent in transposing the various dosages from millicurie-minutes or gram-seconds to reps is appreciated. However, it is felt that this objection is outweighed by the benefit to be derived from a uniform expression of dosage.

APPLICATORS

The physical aspects of the sources of beta rays have been discussed by Hughes[9] and will not be considered here. Any type of applicator is capable of producing some of the effects to be discussed. The radiation cataracts observed clinically and experimentally have been produced by the beta rays of the radon and Sr^{90} applicators.

† Focht, E. F.: Personal communication to the author.

LATE EFFECTS OF BETA RADIATION

The effects of beta radiation that have been observed have appeared up to 15 years following the completion of therapy and have occurred with surface doses of 2,300-33,000 rep. This is within the range of most published dosage schedules. These effects and the approximate doses that produced them are listed in Table 1.

CONJUNCTIVA

Telangiectasis of the Conjunctiva.—This has been observed with surface doses of 3000-5000 rep and usually begins to appear approximately five years after therapy has been completed. It is mainly a cosmetic blemish, producing no significant symptoms. The degree of injection, once fully developed, remains quite constant, being aggravated somewhat by irritating smoke, exposure to sun, and general debility.

TABLE 1.—*Effects of Beta Radiation on the Eye*

Effect	Approximate Dosage (Surface)
Conjunctiva	
Telangiectasis	3000-5000 rep
Keratinization of the epithelium	5,000-10,000 rep
Sclera	
Atrophy	20,000-30,000 rep
Cornea	
Superficial punctate keratitis	5000 rep
Vascularization	20,000-30,000 rep
Scarring	25,000 rep
Uvea	
Iritis	22,000-27,000 rep
Iris atrophy	20,000-30,000 rep
Lens	
Radiation cataract	2,300-22,000 rep

Keratinization of the Conjunctival Epithelium.—This has been observed with doses of 5,000-10,000 rep. Beginning keratinization was observed in one patient treated with 2300 rep, but the process was not sufficiently advanced to produce symptoms. This complication is seen in conjunctival scrapings stained by the Giemsa method and is similar to the changes observed in vitamin A deficiency and in keratitis sicca. It has been noted especially in patients treated with beta radiation for vernal conjunctivitis (vernal

catarrh) and when fully developed has been a serious complication. When the normal mucous membrane of the upper palpebral conjunctiva is converted to a keratinized epithelium, this roughened surface moving over the cornea may produce a punctate keratitis. This results in severe photophobia, lacrimation, and blepharospasm. Treatment is relatively ineffective.

The importance of this sequela is that it persists for life and is often more annoying and debilitating than the original lesion for which treatment was administered. This effect should be given serious consideration when one is advocating any form of superficial therapy for this condition, especially when it is realized that approximately 90% of the cases subside spontaneously with only symptomatic treatment.

We do not believe that the punctate keratitis in these cases is a direct effect of the irradiation, since in most instances no treatment reaches the cornea, owing either to adequate shielding or to the method of administration.

Sclera

Atrophy of the Sclera.—Three cases of scleral necrosis following beta irradiation were reported recently by Jones and Reese.[14] In one case a Sr^{90} applicator was employed and the dose was only 1500 rep. In another case the dose was not known, and in a third it was stated as 1000 mc-min. of radium.‡ This is equivalent to approximately 24,000 rep on the surface. Two additional cases with this complication have been observed. Both were treated with a glass radon bulb. One received approximately 20,000 rep on the surface, and the other, 22,000 rep on the surface. They are described in detail in the case reports.

It is felt that a dose of 20,000-30,000 rep on the surface is most likely to produce this complication.

Cornea

Superficial Punctate Keratitis.—This may be a transient effect of irradiation, lasting four to six weeks with doses up to 5000 rep on the surface. When doses in the order of 20,000 rep on the surface are administered directly over the cornea, this effect has been observed to persist for five months, with all the usual accompanying symptoms. Some relief has been obtained by the use of 0.5%-1% methylcellulose drops or bland ointments. The staining areas may vary in size, shape, and number from time to time and occasionally are sufficiently severe to require patching of the eye for several days. Recurrent ulcerations may occur with minimal or no obvious trauma.

Corneal Vascularization.—Beta radiation has been advocated by others § to eradicate corneal vessels. It has been our experience that doses up to 5000 rep on the surface have little effect on most corneal vessels, especially those resulting from alkali burns. With doses of 20,000-30,000 rep on the surface, we have observed corneal vascularization as a late effect of therapy. This complication may develop up to 12 years after treatment and may be accompanied by varying degrees of corneal scarring.

Corneal Scarring.—This is an infrequent complication of beta irradiation with the usual doses employed. In the Memorial Center group, which are described in detail below, two cases of scarring due to irradiation were observed (Cases 8 and 9). It is our feeling that doses of 25,000 rep or more on the surface are necessary to produce this complication.

Uveal Tract

Iritis.—This complication has been observed in two cases treated with the glass radon bulb with surface doses of 22,000 and 27,000 rep, respectively. In one patient (Case 8) the iritis was undoubtedly secondary to the radiation ulcer, and hence an indirect effect of therapy. In the other patient (Case 4) there was no evidence of uveitis prior to treatment. Within nine days after therapy, the treated eye was markedly injected, the conjunctiva was chemotic, and there was a moderately severe iritis, which persisted for two months.

‡ Treatment in this case was by means of a glass radon bulb.

§ References 4, 6, 9, and 10.

Glaucoma that could with certainty be ascribed solely to the effects of radiation has not been observed.

Iris Atrophy.—This late effect has been observed in four cases with surface doses of 20,000-30,000 rep and appeared from 3½ to 13 years after treatment. If therapy has been applied over a small area, as was the case in the patients observed, the atrophy is localized to that portion of the iris beneath the area of the cornea treated. In one instance this complication was preceded by iritis. The atrophy itself produces no symptoms and has remained stationary in all instances.

Radiation Cataract

This complication of more penetrating radiation is well known and has been the subject of numerous recent investigations.‖ This work has been reviewed excellently by Ham.[20] We have observed eight cases of radiation cataract following beta radiation with doses ranging from 2,300-22,000 rep on the surface.[21] In seven of the eight cases the cataracts have progressed to maturity. The stationary lens opacity resulted from the minimum dose. The time of onset of the cataracts was noted at 3 to 6½ years after treatment in seven of the cases, and in the eighth it was observed after 13 years.

The calculated depth dose at 3 mm. is 230 to 1120 rep. In all cases, the applicator employed was a Monel-filtered bulb, and treatment was applied at or near the limbus. As suggested by von Sallmann,[22] most depth-dose calculations have been made from the center of the cornea to the lens. Actually, most therapy is applied near the limbus, which is considerably closer to the sensitive germinative epithelium of the lens. Experimentally, von Sallmann [22] has shown that radiation cataracts can be produced in rabbits with a Sr^{90} applicator with surface doses of 5000 rep. As he pointed out, the rabbit lens is undoubtedly more radiosensitive than the human lens, but his results demonstrate that the radiations from this type of beta applicator are capable of penetrating sufficiently deep to produce this complication. There is undoubtedly a considerable individual variation in sensitivity to a given dose of radiation. However, the fact that a typical radiation cataract has been observed clinically with as little as 2300 rep on the surface should be given serious consideration in any proposed treatment.

‖ References 15 through 19.

Incidence of Complications

The question arises as to what percentage of patients treated with beta radiation are likely to develop any of the complications mentioned. Many of the cases in which the late effects were observed were treated elsewhere, so that the incidence of complications cannot be estimated. In the Radiotherapy Department of the Institute of Ophthalmology in New York, we have employed grenz rays for the treatment of superficial ocular lesions. Thus, the only consecutive series in which the percentage of complications can be calculated is a group of patients treated at the Memorial Center in New York. This is a small series but does, we believe, give some indication of the incidence of complications that may be expected within the dosage range employed.

Beta radiation has been used in that hospital since the early 1920's. Twelve cases of various types of carcinoma of the conjunctiva and cornea have been treated with a radon bulb—a form of beta radiation. The dose, in millicurie-minutes, has been transposed to roentgen equivalents physical, using the figures of Krohmer.[13] The dose ranged from 11,000 to 33,000 rep on the surface. Ten of these 12 patients have been followed from 2 to 19 years. The other two have not been seen since their treatment and are not included in this series. All the 10 patients have developed one or more of the complications previously described. These were noted 3 to 13 years following therapy and are listed in Table 2, with the number of cases showing each effect and the dosage range.

Ramon Castroviejo, of New York, has noted the late effects of beta radiation, particularly in cases treated for corneal vascularization. In his article,[23] he states:

> When beta rays were used to obliterate vessels as a preliminary step to other surgical procedures,

TABLE 2.—*Late Effects of Beta Radiation and Dosage Range in Ten Cases of Carcinoma of Conjunctiva or Cornea*

Effect	No. of Cases	Per Cent of Total	Dose (on Surface)
Telangiectasis	1	10	16,000 rep (650 mc.-min.)
Atrophy of the sclera *	3	30	20,000-22,000 rep (800-900 mc.-min.)
Superficial punctate keratitis	1	10	27,000 rep (1,100 mc.-min.)
Corneal vascularization	1	10	24,000 rep (1,000 mc.-min.)
Corneal scarring	2	20	24,000-27,000 rep (1,000-1,100 mc.-min.)
Iritis	2	20	22,000-27,000 rep (900-1,100 mc.-min.)
Iris atrophy	4	40	22,000-24,000 rep (900-1,000 mc.-min.)
Radiation cataract	7	70	11,000-22,000 rep (430-900 mc.-min.)

* One of these cases (L. R.) was reported by Jones and Reese.[14]

overdose often resulted in disastrous results, both in keratectomies and in keratoplasties. Very densely vascularized corneal opacities, particularly those observed after burns with vessels involving the cornea throughout its entire circumference, and especially when the eyes remained permanently irritated, with pronounced photophobia, did not respond well to beta radiation therapy, either as the sole method of treatment or as a preliminary to surgery. Enough emphasis cannot be made regarding the undesirable reactions caused by overtreatment with beta rays. I have observed in overtreated cases the following conditions requiring enucleation: absolute glaucoma; persistent unbearable irritation; perforation of the cornea with endophthalmitis, and greatly delayed healing of the graft with the formation of fistulae. I insist very strongly on this point of avoiding overtreatment by irradiation, because the complications discussed have been in patients treated by individual physicians and organizations who reported never to have observed such complications in their cases.

When one is treating a malignant tumor, the possible effects of irradiation are relatively inconsequential as compared with the life of the patient. Most of the lesions for which beta irradiation is advocated currently are benign. Thus, the possible sequelae of such therapy assume paramount importance. Before deciding upon this form of treatment, one should always ask this question: "Will the possible late effects of therapy be more serious than the disease being treated?"

REPORT OF CASES

CASE 1.¶—This 56-year-old white woman was treated for precancerous melanosis (proved by biopsy) of the left bulbar conjunctiva with 3000 rep on the surface to each of three areas. Treatment was administered by means of a glass radon bulb. Figure 1 shows the resulting telangiectasis, which appeared 11 years after therapy was completed. A recurrence necessitated subsequent exenteration.

This complication of therapy is relatively inconsequential in this case as compared with the lesion treated. However, in benign lesions, especially ones that can be satisfactorily treated by other means, the possibility of this unsightly late radiation effect should be given due consideration.

¶ Case 1 is a patient of Dr. A. B. Reese, New York, and is used with his permission.

Fig. 1 (Case 1).—Telangiectasis of the bulbar conjunctiva, which appeared 11 years after treatment with 3000 rep on the surface to each of three areas.

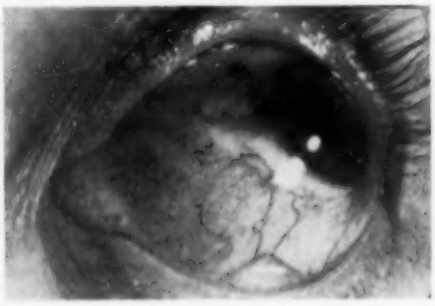


Fig. 2 (Case 2).—External appearance of the left eye following beta irradiation in childhood for vernal conjunctivitis (vernal catarrh). The blepharospasm is apparent.

Fig. 3 (Case 2).—Appearance of the conjunctiva of the left upper lid of the patient shown in Figure 2. Scrapings showed keratinization of the epithelium. A punctate keratitis is also present.

CASE 2.—The left eye of this white man was treated in childhood for vernal conjunctivitis (vernal catarrh) by means of a radium plaque applied over the skin surface. The exact dose is unknown. From the appearance of the skin and the fact that the cilia are intact, the dose undoubtedly was within the range presently advocated for the treatment of this condition. Figure 2 shows the external appearance of the lids. The slight tanning of the skin and the blepharospasm are apparent. Figure 3 shows the telangiectasis and scarring of the palpebral conjunctiva. Scrapings of the conjunctiva revealed keratinization of the conjunctival epithelium. The cornea showed a punctate keratitis. This was the result of the roughened lid rubbing on the cornea and explains the patient's photophobia and blepharospasm. This complication of irradiation will persist for life and is a source of constant irritation.

CASE 3.—This 45-year-old Negro woman was seen at the Memorial Center, New York, with a 2×2 mm. pigmented lesion on the nasal bulbar conjunctiva of the right eye. Biopsy tissue from a similar lesion on the temporal bulbar conjunctiva was diagnosed as melanoma. The area nasally received a total of 800 mc-min. with a radon glass bulb in two treatments at monthly intervals. This amount represents a total surface dose of approximately 20,000 rep. Five years and three months after treatment, a radiation cataract was first noted. This has progressed to maturity. Nine years and two months after the last treatment an area of scleral necrosis was observed. She has been followed for 18 years and 9 months, and there is no evidence of recurrent disease. The affected area in the sclera shows a fairly well-demarcated, circular dehiscence, through which uveal tissue can be seen. The defect is filled with a yellowish, opaque material which is extremely hard, is very adherent to the underlying tissue, and projects above the surrounding conjunctival surface. Figure 4 shows this area nasally, as well as the nearly mature radiation cataract. An attempt was made to remove a portion of this material for histologic study. It had the feeling of calcium to the knife, and only tiny fragments could be flecked off the surface. It was deemed unwise to attempt to excise the mass entirely, for fear of perforating the globe.

CASE 4.—This 59-year-old white man was first seen in Vanderbilt Clinic of the Presbyterian Hospital, New York, with a shiny, white, raised lesion with an irregular surface occupying the temporal limbus of the left eye. A diagnosis of Bowen's disease was made by biopsy, and he was referred to the Memorial Center, New York, for therapy. The tumor was irradiated with a radon glass bulb. The area was divided into three parts, each area receiving 900 mc-min. (approximately 22,000 rep on the surface). There was an intense reaction to therapy accompanied by iritis, which persisted for two months. He has been followed eight years and two months. The area treated shows considerable ischemia. A radiation cataract, which has progressed to maturity, was observed four and one-half years after treatment. Approximately five and one-half years after therapy, the eye became red and painful, and an area of ulceration was noted in the sclera near the limbus at 3:30 o'clock. This healed during the next month, leaving an area in the sclera through which the uvea could be seen.

Accompanying the ulcer was an iritis, which persisted for about three months and resulted in a few posterior synechiae temporally. As this quieted down, the iris temporally was noted to be atrophic. The area of scleral necrosis gradually enlarged, and on one occasion the local ophthalmologist attempted to remove a firm mass from its center.

The mechanism by which this focal scleral necrosis is produced is not understood at this time. A tumor may result in some thinning of the sclera, but this should become apparent soon after therapy, when the neoplasm has disappeared. In both of the

Fig. 4 (Case 3).—Appearance of the right eye 18 years after treatment of a melanoma of the nasal bulbar conjunctiva. Total dose was 20,000 rep on the surface. The scleral necrosis and cataract are apparent.

Fig. 5 (Case 5).—The left eye prior to operation, showing the vascularized leucoma.

cases the necrosis was localized and appeared several years after the treatment. Also, in both instances the dehiscences were partially replaced by a firm material resembling calcium. It is believed, therefore, that these areas represent a late effect of irradiation.

Case 5.#—This 50-year-old white man gave a history of recurrent bilateral corneal ulcers and iritis for many years, treated by local medication, curettage, and conjunctival flaps. Vision when he was first seen was 10/400 O. D. and hand motion at 1 ft. O. S. Examination showed bilateral vascularized leucomas.

Figure 5 shows the left eye preoperatively. The dense vascularized leucoma is apparent. The following day a superficial keratectomy was done. This was followed by 650 r of x-rays (factors unknown), with no effect on the corneal vascularization. During the next seven months beta radiation was given with a radon applicator to six areas around the limbus. The total calculated dose on the surface was 22,000 rep, given in four treatments. Figure 6 shows the appearance of the left eye nine months after the completion of the beta radiation therapy. The scarring and vascularization are considerably less. At this time the result would appear to be successful. The limbal radiation ischemia is apparent, however. Three days later an 8 mm. penetrating keratoplasty was done. Figure 7 shows the eye four months after this last operation. The result is still satisfactory, although the graft is quite hazy. The nasal and temporal limbal areas show some ischemia, and there are numerous vessels temporally in the host cornea. Figure 8 shows the eye two years after the keratoplasty. The marked telangiectasis of the conjunctiva and the vascularization of the cornea are in large part radiation changes. The latter has resulted in clouding of the graft. Approximately 11 days after this last photograph a total penetrating keratoplasty (10.5 mm.) was performed in an effort to improve the vision. A complete iridectomy was done and the lens extracted. Figure 9 shows the eye six weeks after the last operation. The poor union of the graft and the host

Cases 5, 6, and 7 are patients of Dr. Ramon Castroviejo, New York, and are used with his permission.

Fig. 7 (Case 5).—Same eye as that shown in Figure 6 four months later. Numerous vessels are present in the host cornea.

Fig. 6 (Case 5).—Appearance of the same eye as that shown in Figure 5 nine months after a superficial keratectomy and beta irradiation. Three days later a penetrating keratoplasty was performed on this eye.

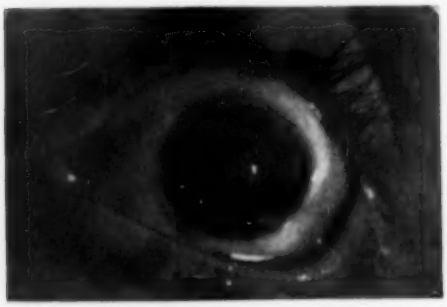


Fig. 8 (Case 5).—Appearance of the eye shown in Figure 6 two years later. The late radiation changes are becoming apparent. Eleven days later a total penetrating keratoplasty was performed.

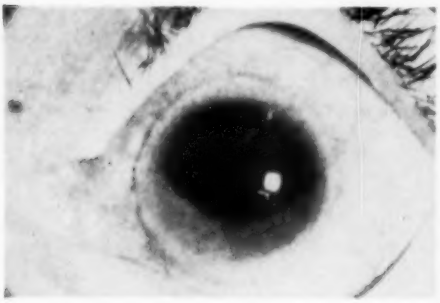


Fig. 9 (Case 5).—Appearance of the eye shown in Figure 8 six weeks after the last operation.

cornea is apparent nasally and below. Because of a rise in tension, a cyclodiathermy was performed. The secondary glaucoma was not related to the beta radiation therapy. Two conjunctival flaps were subsequently brought over the nasal edge of the graft in an effort to promote healing. Figure 10 shows the eye six months after the total keratoplasty. The fistula is apparent at 11 o'clock, and the graft has become more opaque. The eye was constantly irritated and three months later was enucleated.

The poor healing was felt by Dr. Castroviejo to be due to excessive radiation, and similar cases of his have confirmed this opinion. It is our feeling at present that therapy should be reserved solely for postoperative use. If radiation is given preoperatively, even in conservative doses, the vessels obliterated frequently reappear under the stimulus of surgery, and additional therapy may be inadvisable.

Case 6.—This 40-year-old white man had a history of repeated attacks of kerato-iritis since the age of 5 years. Fifteen years before he was first seen, an optical iridectomy was done on the right eye, without improvement in vision. Seven years

Fig. 10 (Case 5).—Appearance of the same eye as that shown in Figure 8 six months later. The fistula at 11 o'clock is apparent. Three months later the eye was enucleated.

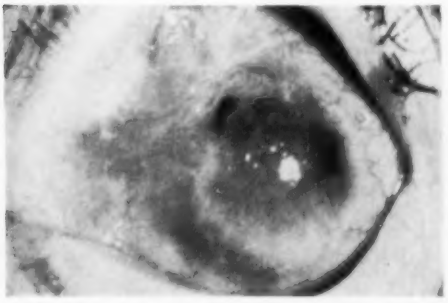
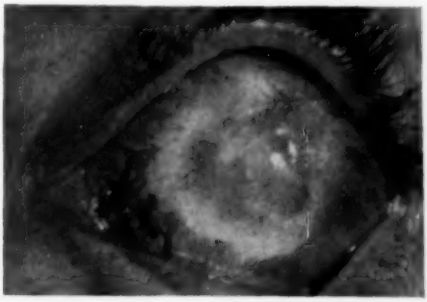


Fig. 11 (Case 6).—Appearance of the eye one year after receiving 30,500 rep on the surface to eight areas around the limbus. The ischemia and beginning telangiectasis are apparent.

before he was first seen, a corneal transplantation was done on this eye, and three years later a second, similar operation was performed, with no visual improvement. During the year before his first visit beta radiation was given with a radium D applicator to eight areas around the limbus of the right eye. Each area received one treatment (2400-5100 rep), and the total dose on the surface was 30,500 rep. The vision in the right eye was counting fingers at 1 ft. Figure 11 shows the appearance of this eye approximately one year after irradiation was completed. The postirradiation ischemia around the limbus is apparent, as well as the beginning telangiectasis. The ischemia will prevent adequate healing after surgery and makes further treatment inadvisable.

Case 7.—This patient was seen in consultation regarding a corneal transplantation. A vascularized leucoma of the left cornea had been treated with beta radiation. The type of applicator and dosage are unknown. Irradiation had succeeded in obliterating the corneal vessels but had made the eye unfit for surgery. Figure 12 shows the late appearance of this eye, after excessive radiation. The telangiectasis, the limbal ischemia, and the marked corneal scarring are apparent.

Fig. 12 (Case 7).—Late appearance of an eye following excessive beta irradiation.



Case 8.—This 65-year-old white woman was first seen at the Memorial Center, New York, with a small, round lesion involving the temporal bulbar conjunctiva, adjacent to the limbus of the right eye at 9 o'clock. The lesion was excised, and the pathologic report was epidermoid carcinoma, Grade 2. Two weeks later, the area was given 1100 mc-min. (approximately 27,000 rep on the surface) with a radon glass bulb. Therapy was applied with motion over the involved area. Four weeks later there was a deep, ischemic ulcer, with no evidence of infection, in the treated area. One month later the adjacent cornea became cloudy but did not ulcerate. The conjunctival ulcer healed in two months, but the corneal nebula persisted during the two-year period in which the patient was observed. She has since been lost to follow-up.

It is impossible to calculate exactly the amount of radiation the cornea received by the method of administration. However, since the cornea was not involved in the original surgical procedure and since there was no evidence of infection at any time, it is our feeling that the corneal opacity could have been secondary to the beta radiation therapy.

Case 9.—This 50-year-old Negro woman was first seen in the Vanderbilt Clinic of the Presbyterian Hospital, New York, with an elevated, pigmented tumor on the temporal side of the left cornea. Biopsy proved it to be a melanoma, and the patient was referred to the Memorial Center, New York, for beta radiation. The area was given 100 mc-min. with a radon glass bulb (approximately 24,000 rep on the surface). Within the next two months the lesion gradually disappeared, leaving the cornea in this area markedly pigmented. Four years and five months after treatment superficial scarring was observed, in which there was a vertical, oval ulcer but no evidence of recurrent disease. The ulcer persisted, and when it was observed nine months later, its center showed atheromatous changes. The patient reported that occasionally a firm material would fall out of the affected area. Nineteen months after its appearance the ulcer finally healed, leaving an irregular, scarred surface, which produced a foreign body sensation at times. Twelve years after therapy the scar showed some calcification and was moderately vascularized.

Other late radiation changes observed in this eye were a cataract, which appeared five years and six months after treatment and which progressed to maturity, and an area of iris atrophy temporally under the area treated, which appeared six and one-third years after therapy.

Case 10.—This 66-year-old white man received 2300 rep on the surface to the right nasal bulbar conjunctiva for the treatment of a lymphosarcoma of the conjunctiva. Therapy was administered with a Monel-filtered applicator. Examination five years after treatment showed a typical early radiation cataract nasally beneath the treatment area. Vision is 20/15. Figure 13 shows the slight telangiectasis in the treatment area. Scrapings showed some keratinization of the epithelium, which was not sufficient to produce symptoms. This case may be one of unusual radiation sensitivity, since the other beta radiation cataracts observed have resulted from doses of 10,000 rep or more on the surface. Nevertheless, it does call attention to the fact that small doses with this type of applicator are capable of producing this complication.

SUMMARY

Conservatism in the use of beta radiation in superficial ophthalmic lesions is urged, inasmuch as numerous late effects have been observed. These are telangiectasis of the conjunctiva, keratinization of the conjunctival epithelium, atrophy of the sclera, superficial punctate keratitis, corneal vascularization, corneal scarring, iritis, iris atrophy, and radiation cataract.

It is suggested that the current high-dosage schedules be reduced. It is felt that doses of 2000-3000 rep on the surface would be more judicious and that a surface dose of 5000 rep should seldom be exceeded in the treatment of benign lesions.

Fig. 13 (Case 10).—Appearance of an eye five years after receiving 2300 rep on the surface of the nasal bulbar conjunctiva. A radiation cataract is present.

635 W. 165th St. (32).

REFERENCES

1. Desjardins, A. U.: Action of Roentgen Rays and Radium on the Eye and Ear: Experimental Data and Clinical Radiotherapy, Am. J. Roentgenol. **26**:639, 787, 921, 1931.

2. Woods, A. C.: Treatment of Tuberculosis of the Anterior Portion of the Eye with Beta Rays of Radium, Arch. Ophth. **22**:735, 1939.

3. Burnam, C. F., and Neill, W. J.: Use of Beta Ray of Radium Applicator: Description of Method and Results Obtained in Superficial Lesions of the Eye, South. M. J. **33**:279, 1940.

4. Iliff, C. E.: Beta Irradiation in Ophthalmology, Arch. Ophth. **38**:415, 1947.

5. Swanberg, H.: A New Ophthalmic Applicator for Pure Beta Irradiation Utilizing Radium D, Mississippi Valley M. J. **70**:71, 1948.

6. Ruedemann, A. D.: Beta Radiation Therapy, Arch. Ophth. **41**:1, 1949.

7. Friedell, H. L.; Thomas, C. I., and Krohmer, J. S.: Description of a Sr^{90} Applicator and Its Use on the Eye, Am. J. Roentgenol. **65**:232, 1951.

8. Wilson, F. M., and Wilson, J. W.: Radioactive Strontium Therapy of the Eye: Corneal Biostandardization and Evaluation of an Applicator for Use in Ophthalmology, A. M. A. Arch. Ophth. **48**:686, 1952.

9. Hughes, W. F., Jr.: Beta Radiation Therapy in Ophthalmology, Tr. Am. Ophth. Soc. **50**:469, 1952.

10. Friedell, H. L.; Thomas, C. I., and Krohmer, J. S.: Evaluation of the Clinical Use of a Strontium 90 Beta Ray Applicator with a Review of the Underlying Principles, Am. J. Roentgenol. **71**:25, 1954.

11. Desjardins, A. U.: Radiosensitiveness of Cells and Tissues and Some Medical Implications, Arch. Surg. **25**:926, 1932.

12. Ellinger, F.: Biologic Fundamentals of Radiation Therapy, Amsterdam, Elsevier Pub. Co.; New York, Nordeman Publishing Company, Inc., 1941.

13. Krohmer, J. S.: Physical Measurements in Various Beta Ray Applicators, Am. J. Roentgenol. **66**:791, 1951.

14. Jones, I. S., and Reese, A. B.: Focal Scleral Necrosis, A. M. A. Arch. Ophth. **49**:633, 1953.

15. von Sallmann, L.: Experimental Studies on Early Lens Changes After Roentgen Irradiation: I. Morphological and Cytochemical Changes, A. M. A. Arch. Ophth. **45**:149, 1951.

16. von Sallmann, L., and Locke, B. D.: Experimental Studies on Early Lens Changes After Roentgen Irradiation: II. Exchange and Penetration of Radioactive Indicators (Na^{24}, K^{42}, I^{131}, P^{32}) in Normal and Irradiated Lenses of Rabbits, A. M. A. Arch. Ophth. **45**:431, 1951.

17. Cogan, D. G., and Donaldson, D. D.: Experimental Radiation Cataracts, A. M. A. Arch. Ophth. **45**:508, 1951.

18. von Sallmann, L.: Experimental Studies on Early Lens Changes After Roentgen Irradiation: III. Effect of X-Radiation on Mitotic Activity and Nuclear Fragmentation of Lens Epithelium in Normal and Cysteine-Treated Rabbits, A. M. A. Arch. Ophth. **47**:305, 1952.

19. Clapp, C. A.: Effect of X-Ray and Radiation upon the Crystalline Lens, Am. J. Ophth. **15**:1039, 1952.

20. Ham, W. T., Jr.: Radiation Cataracts, A. M. A. Arch. Ophth. **50**:608, 1953.

21. Merriam, G. R., Jr.: Clinical Report on Radiation Dosages Producing Cataract, to be published.

22. von Sallmann, L.; Munoz, C. M., and Drungiz, A.: Effects of Beta Irradiation on the Rabbit Lens, A. M. A. Arch. Ophth. **50**:727, 1953.

23. Castroviejo, R.: Beta Radiation Therapy for Corneal Vascularization, L'Année thérapeutique en ophtalmologie, Tome 4, p. 299, 1953.

Edrophonium (Tensilon) in Diagnosis of Ocular Myasthenia Gravis

S. ARTHUR BORUCHOFF, M.D., Boston
and
BERNARD GOLDBERG, M.D., New York

Myasthenia gravis frequently involves the extraocular muscles. Indeed, eye muscle involvement may be the earliest or the only sign of myasthenia gravis. The following history is presented to portray such a case and to call to the attention of the ophthalmologist a new drug for the diagnosis of myasthenia gravis thus far unknown to the ophthalmologic literature.

From the service of Dr. Truman L. Boyes and the Department of Research, New York Eye and Ear Infirmary.

Current address: Institute of Ophthalmology, Judd St., London, W. C. 1, England (Dr. Boruchoff).

Fig. 1.—Before edrophonium (Tensilon). Patient in gaze to the left. Note marked ptosis of the right upper lid and inability to adduct the right eye. Courtesy of Mr. John P. Goeller, Photographer, New York Eye and Ear Infirmary.

Fig. 2.—Fifteen seconds following beginning of injection of 10 mg. of edrophonium. Note disappearance of ptosis and marked improvement in ability to adduct the right eye. Courtesy of Mr. John P. Goeller, Photographer, New York Eye and Ear Infirmary.

REPORT OF A CASE

J. C., a 16-year-old white boy, was first seen at the Outpatient Clinic of the New York Eye and Ear Infirmary on July 30, 1953, complaining of "bloodshot eyes." Visual acuity was recorded at 20/20 O.U. Physical examination revealed bilateral bulbar conjunctival injection with no other abnormalities: Lids, media and fundi were normal. Pupillary reactions were normal. No abnormality of the extraocular musculature was noted. The conjunctivitis cleared rapidly and completely on a local chemotherapeutic regimen. He was next seen on May 5, 1954, at which time he complained of increasingly severe drooping of the upper lids and occasional double vision of approximately three months' duration. Because of the presence of external ophthalmoplegia and ptosis, the patient was admitted for study.

The general medical examination was entirely negative. The only abnormality noted was ocular:

There was bilateral ptosis, more marked on the right, and the eyes were in a position of constant exotropia of about 60△, with free alternation of fixation. The vision was unchanged from the previous examination. There was an external ophthalmoplegia with involvement of both medial rectus and partial involvement of both lateral rectus muscles. Vertical motion was partially impaired O. U. The pupils reacted promptly to light; the accommodation reflex was present, and the fundi were normal. Consultation with the E. N. T. and neurology services failed to reveal any further abnormality. C. B. C., urine, fasting blood sugar, serology, sedimentation rate, and B. M. R. were normal, as were the central and peripheral fields and x-rays of the skull, chest, and teeth.

The response to an adequate test dose of neostigmine (Prostigmin) was equivocal. The patient was then given an intravenous injection of edrophonium (Tensilon) chloride, 10 mg. (1 cc.). Within one minute, the patient was able to raise both lids (Figs. 1 and 2), and the extraocular movements except for adduction of the O. S. became normal. The effect of the injection began to recede after two minutes, and was completely expended in five minutes. The patient is being treated with oral neostigmine bromide, 30 mg. q. i. d., and is somewhat improved on this regimen, although some ptosis and exotropia persist.

COMMENT

Edrophonium chloride (Tensilon; Hoffmann-LaRoche, Inc.) is a quaternary ammonium compound. Although it has some action as an anticholinesterase compound, its primary mode of action is direct stimulation of the myoneural junction.[1] Originally introduced as an antagonist of curare-like agents, it was found to have an important role in the diagnosis of myasthenia gravis and in the treatment of the crises of myasthenia gravis.[2]

Within seconds following the injection of edrophonium, the myasthenic patient recovers a remarkable degree of strength in his affected muscles without fasciculations being noted; a nonmyasthenic subject similarly treated will experience no increase in strength, and fasciculations are seen.[3] The onset of action of the drug begins within 30 seconds (often before the injection is complete); it reaches its maximum effect within 1 to 10 minutes, and declines thereafter. Side-effects are infrequent; transient lacrimation, distorted vision, and a "cramping" sensation of the eyes and lids, all of mild degree, may be noted. No side-effects were noted in the case reported above.

SUMMARY

Edrophonium provides the ophthalmologist with a safe, rapid diagnostic test for the investigation of cases of suspected myasthenia gravis. The positive response is dramatic, and a myasthenic who gives a negative response on testing with neostigmine may respond dramatically to edrophonium.

REFERENCES

1. Macfarlane, D. W.; Pelikan, E. W., and Unna, K. R.: Evaluation of Curarizing Agents in Man: V. Antagonism of Curarizing Effects of d-Tubocurarine by Neostigmine, m-Hydroxyphenyltrimethylammonium and m-Hydroxyphenylethyldimethylammonium, J. Pharmacol. & Exper. Therap. **100**:382, 1950.

2. Westerberg, M. R.; Magee, K. R., and Shideman, F. E.: Effect of Tensilon in Myasthenia Gravis, Neurology **3**:302, 1953.

3. Osserman, K. E.; Kaplan, L. I., and Besson, G.: Studies in Myasthenia Gravis: Edrophonium Chloride (Tensilon) Test as a New Approach to Management, J. Mt. Sinai Hosp. **20**:165, 1953.

Clinical Notes, New Instruments and Techniques

FIXATION FORCEPS

ALFRED A. NISBET, M.D., San Antonio, Texas

THIS instrument is a rustless-steel thumb forceps curved about 90 degrees, as shown in the accompanying three-quarter-scale illustration. The forceps is available with either spring or sliding catch, which makes it self-retaining. The serrated, interdigitating jaw margins face on the convex curve at its distal end. The jaws are 4 mm. in length.

This forceps was made to my specifications about seven years ago and has been found useful for rotating the globe in strabismus and cataract surgery. It may be applied easily because the jaw margins are located on the outer side of the curve. Bulbar conjunctiva alone, or a rectus muscle in addition, may be grasped. An advantage gained is that there is less twisting of and trauma to tissue held by the jaws while the eye is in the rotated position.

This forceps may be obtained from the Storz Instrument Company.

News and Comment

SOCIETY NEWS

Midwest Section, Association for Research in Ophthalmology.—The Midwest Section of the Association met on Saturday, April 30, 1955, at the Mayo Clinic, Rochester, Minn. A tour of the Medical Sciences Building and the new Mayo Clinic Diagnostic Building began at 9 a. m. at Mann Hall, Medical Sciences Building, 321 Third Ave., S. W. Luncheon was served at 11:30 in Mann Hall; the scientific session began at 12:30 p. m.

The program follows:

Albert E. Zeller: Some Aspects of Phenol Coupling in the Cornea and Vitreous

Walter H. Fink: The Nonstriated Muscle of the Human Orbit

A. C. Hilding: Some Aspects of Healing of the Posterior Surface of the Cornea Following Cataract Surgery

A. H. Riesen: Early Developments of Fixation Responses as Related to the Visual Environment

Christopher H. Moore: Effects of Ultrasound upon Certain Structures of the Eye

H. A. Swanljung and Frederick C. Blodi: Tonography in Provocative Tests for Glaucoma

A. K. Hansen and H. A. Swanljung: Observations on the Investigation of Anomalous Retinal Correspondence

Lee Allen and Hermann M. Burian: New Concepts of Development of the Angle of the Anterior Chamber: Studies of Its Embryology and Comparative Anatomy

B. Schwartz and P. J. Leinfelder: Effect of Change in pH on the Lens Metabolism

E. A. Auerbach and Hermann M. Burian: Electroretinographic Evidence for the Scotopic Curve During the Photopic Phase of Dark Adaptation

PAUL W. MILES, Chairman
ARLINGTON C. KRAUSE, Vice-Chairman
FRANK W. NEWELL, Secretary

Registry of Interesting Cases

It is the purpose of this section to record cases on the basis of interest only. No complete review of the literature is attempted and no claim for priority is implied except when specifically stated. Publication of case reports is subject to the concurrence of the Editorial Board on the interesting aspects of the case. It is requested that the reports submitted be as brief as is consistent with inclusion of the pertinent facts, bear a title that is as specific as possible, be prefaced by a paragraph that states why the author feels the case is of interest and be accompanied with photographs whenever possible.

SERUM SICKNESS MANIFESTED BY ANTERIOR CHAMBER EXUDATE

SERUM sickness generally develops 7 to 12 days after exposure to the allergen and is transitory. Nine days after receiving tetanus antitoxin this patient developed an exudative reaction with no inflammatory signs in one anterior chamber. It improved rapidly with a minimum of therapy. A presumptive diagnosis of serum sickness can be made in this case on the basis of the time of appearance and on the transitory character of the disease. I could find no record of such a lesion in the literature.

REPORT OF CASE

H. G., a white man, age 29, was bitten by a dog on May 22, 1954. At 3 p. m. on May 23 he was given tetanus antitoxin at the local hospital. He began to have signs and symptoms within an hour. He returned to the hospital at 7 p. m. (four hours after the injection), at which time he had urticaria; swelling and aching of his knees, ankles, elbows; aching of his hips; pruritus; chest pain, and difficult breathing. The intern treated him with methapyrilene (Histadyl), epinephrine, corticotropin, and hydrocortisone. The next day he was discharged. On June 1 he had pain in the left eye and marked blurring. The pain left shortly but the blurring remained. When he was examined on June 4, his vision was 20/20 O.D. and less than 20/100 O.S. There was no conjunctival or circumcorneal injection. The pupil reacted well to light. Slit-lamp examination revealed that the posterior surface of the cornea was heavily covered with a fine granular precipitate. He was given atropine to use, and when he was seen a week later, his vision was better than 20/40 and the precipitate was practically gone.

MARK THUMIM, M.D.
Professional Building, Middletown, Conn.

News and Comment

GENERAL NEWS

Joint Ophthalmology and Otolaryngology Meeting, Atlantic City.—The Annual Meeting of the Pennsylvania Academy of Ophthalmology and Otolaryngology in conjunction with the New Jersey Society of Ophthalmology and Otolaryngology, the New Jersey Ophthalmological Society, and the West Virginia Academy of Ophthalmology and Otolaryngology will be held at the Hotel Traymore, Atlantic City, N. J., on May 18, 19, 20, and 21, 1955.

A scientific program has been planned, with emphasis on instructional courses and study clubs to bring out practical points in ophthalmology and otolaryngology.

Details of the meeting will be sent to all members of the various societies in the spring issue of the *Transactions of the Pennsylvania Academy of Ophthalmology and Otolaryngology*, to be published in April. In the meantime, interested persons are urged to write directly to the Hotel Traymore for hotel reservations.

Inquiries regarding the meeting should be addressed to Daniel S. DeStio, M.D., 1006 Highland Building, Pittsburgh 6.

SOCIETY NEWS

Georgia Society of Ophthalmology and Otolaryngology.—At the spring meeting of the Georgia Society of Ophthalmology and Otolaryngology in Savannah recently the following officers were elected: president, Alton V. Hallum, M.D., Atlanta; vice-president, W. L. Barton, M.D., Macon, and secretary-treasurer, W. P. Rhyne, M.D., Albany.

Annual Reviews

DISEASES OF THE RETINA AND OPTIC NERVE

HENRY P. WAGENER, M.D., Rochester, Minn.

RETROLENTAL FIBROPLASIA

THE CONTINUED interest of ophthalmologists in the problem of retrolental fibroplasia is evidenced by the large number of papers on the subject that appeared during 1954. Many of these papers present evaluation of the effects of administration of oxygen to premature infants. As noted by Odell,[1] most of the controversy regarding the cause of retrolental fibroplasia centers around two major concepts of the basic lesion, namely: (1) The primary disturbance is vascular, as a result of oxygen toxicity or anoxia of the retina, and (2) edema of the retina develops primarily as a result of imbalance of electrolytes from the feeding of cow's milk. Odell considers that neither factor has been definitely established as the cause in all cases.

Duke-Elder[2] thinks that anoxia of the retina is the basic cause of retrolental fibroplasia. He noted that about 50% of such patients who were blind showed some evidence of cerebral trauma, probably from anoxia; they were mentally retarded or deficient. In an attempt to determine whether mental retardation in children with severe retrolental fibroplasia is due to loss of vision or to cerebral damage, Jim and Krause[3] studied the electroencephalograms of 15 patients ranging in age from 4 months to 10 years. They did not find any definite pattern or consistent abnormality. The alterations in the pattern of the electroencephalogram during stimulation of the eyes by light did not indicate whether or not perception of light was present.

Pathology.—Ashton[4] defines retrolental fibroplasia as a primary retinal disease of noninflammatory origin resulting from disordered retinal vascularization. He divides it pathologically into three stages: (1) proliferation of vasoformative tissue in the inner layers of the retina with beginning eruption of the tissue through the internal limiting membrane into the vitreous; (2) commencing retinal detachment with formation of fibrous strands in the vitreous, and (3) total retinal detachment and formation of a dense retrolental fibrous membrane. He states that he has not seen retrolental fibroplasia in a fully matured infant.

Cicatricial Stage.—Reese and Stepanik[5] state, however, that retrolental fibroplasia does occur in infants of normal birth weight. They found lesions in 36 eyes of 20 infants with birth weights between 5 and 8 lb. (2268 and 3629 gm.). They present an analysis of their findings in the eyes of 672 infants with retrolental fibroplasia in the inactive phase. Lesions were found in 1277 of the 1344 eyes examined and were of Grade 5 (in which the retrolental tissue covers the entire pupillary area) in 62%; 32 eyes were found to be normal. Dentate or ciliary processes were noted in 21%, retinal folds and localized detachment in 6%, microphthalmos in 10%, buphthalmos in 3%, and cataract in 3%.

Incidence in Relation to Administration of Oxygen.—Owens[6] found some manifestation of acute retrolental fibroplasia in one or both eyes in 73 of 128 infants (57%) who had birth weights less than 1360 gm. (3 lb.).

From the Section of Ophthalmology, Mayo Clinic and Mayo Foundation.

The Mayo Foundation, Rochester, Minn., is a part of the Graduate School of the University of Minnesota.

However, the acute phase regressed without visible residuals in 44%, and a partial or complete retrolental membrane formed in only 19 patients (26%). Because of this striking tendency to spontaneous regression, Owens states that proper evaluation of the incidence of retrolental fibroplasia and the effects of treatment requires separate listing of acute and residual lesions.

Locke [7] noted acute lesions in 60 of 160 premature infants (37%) kept in a high-oxygen environment for 10 to 30 days; in 18 (11%) the lesions were severe. Among 124 prematures to whom oxygen was administered in minimal amounts, only 2 (1.6%) had acute lesions, which regressed completely in both.

Gordon and associates [8] divide their observations on 211 prematures into four periods according to the amount of oxygen administered. During the first period of "unscrutinized" but probably moderate use of oxygen, residual lesions were found in 15% of 80 infants and retrolental membranes in 10%. During the second period of "unscrutinized" use of oxygen in concentrations of 60% or more, residual lesions were found in 45% of 20 infants and retrolental membranes in 35%. During the third period (transition to administration of oxygen in lower concentration), residual lesions were found in 29% of 14 infants and retrolental membranes in 21%. During the fourth period (oxygen concentration not more than 40% and shorter periods of administration), residual lesions were found in 8% of 97 infants and retrolental membranes in 2%.

Patz * observed over a six-month period 120 prematures to whom oxygen was administered on an alternate-admission basis in either high concentration (60 to 70% for 28 days or longer) or low concentration (less than 40% and only for specific clinical indications). Of the "high" group, 21 (35%) had Stage 1 or 2 lesions, which regressed completely, but 12 (20%) had advanced retrolental fibroplasia. Of the "low" group, nine (15%) had Stage 1 or 2 changes, which regressed completely, and only one (1.7%) had advanced retrolental fibroplasia. All the lesions in the "high" group developed during continuous administration of oxygen.

Forrester and co-workers [11] record the disappearance of retrolental fibroplasia from two nurseries for premature children in Manchester, England. They studied 83 patients who had this disease during a six-year period; 36 had "permanent changes," with detectable lesions aside from myopia or vascular tortuosity after the age of 6 months, and 21 were blind. During the years 1947 and 1948, they saw only one such patient. During the years 1950 and 1951, they found 32 patients with "permanent changes"; 20 were blind. During the years 1952 and 1953, they found only three patients with "permanent changes"; none were blind. The last infant with any "permanent change" was born in June, 1952. They state that, since October, 1951, the amount of oxygen used for each infant has been severely restricted and that, since November, 1951, there has not been a case of blindness due to the disease; the incidence of transient lesions has been reduced also. They state, "These observations confirm the important role that oxygen plays in transforming a rare sporadic disease into a major cause of blindness."

Lanman and associates [12] compare their findings in 36 prematures to whom 69% oxygen was administered for a minimum of two weeks and then withdrawn abruptly with the findings in 28 to whom oxygen was given only when needed for the relief of cyanosis. Of the first group, 22 (61%) experienced the vascular stage of retrolental fibroplasia and 8 (22%) went on to the cicatricial stage. Of the second group, two (7%) had the vascular stage and none went on to the cicatricial stage.

Bedrossian and co-workers [13] agree that prolonged use of oxygen in high concentrations predisposes to the disease, but they think that the commonest precipitating factor is too rapid withdrawal of supplemental oxygen. The lesions in 68 of 74 patients they observed developed after use of supplemental oxygen was stopped. Of 25 infants who were

* References 9 and 10.

given 60% oxygen and not gradually weaned, 13 (52%) had retinopathy; of 24 infants who were given 50% oxygen and gradually weaned, only 2 (8%) had retinopathy. These authors made the interesting observation that retinal detachment occurring in the retinopathy of prematurity is not irreversible. Detachment was present in 49 of their 74 patients; it receded completely in 20.

Fortier [14] notes that, in the giving of high concentrations of oxygen to premature infants, "the oxygen-carbon dioxide balance which is important in the regulation of vasomotor balance in prematurity has been ignored." He suggests that the addition of carbon dioxide in nontoxic proportions to the oxygen administered might prevent the constriction of the retinal vessels that leads to retrolental fibroplasia.

Clinical Evidence Against the Hyperoxia Theory.—Fontaine [15] observed 144 cases of retinopathy among 1019 prematures weighing less than 2000 gm. at birth. Complete regression occurred in 90 (63%); complete retrolental fibroplasia and blindness resulted in 40 (28%). Complete fibroplasia developed in 6% of the patients who received large amounts of oxygen and in 8% of those who received small amounts. Hart [16] states that, in spite of the generous use of oxygen, only 1 case of retrolental fibroplasia was observed among 473 infants. Usually the concentration of oxygen was gradually reduced.

Denti and Bernardi [17] state that the retinopathy of prematurity was unknown in Italy before March, 1953. They found 36 cases among 122 prematures; 26 had received intensive oxygen therapy, but 10 had received little or no oxygen. Complete retrolental fibroplasia developed in only 1 patient, although detachment of the retina occurred in 10.

After critical analysis of the cases of retrolental fibroplasia occurring in the Boston Lying-in Hospital, Zacharias and co-workers [18] state that their observations "fail to support the idea that oxygen therapy, when measured in duration, is a major or even a necessary causal factor in the occurrence of this disease." They note "an abrupt fall in the incidence of *severe* cases in 1949, in spite of the fact that oxygen therapy of long duration (an average of 23 days) was used during that year." Also, "no conspicuous change in incidence or severity occurred in 1951 following a marked reduction in the duration of oxygen therapy."

Pathogenesis.—Blodi [19] states that the pathogenesis of retrolental fibroplasia remains unknown and that it has not been determined as yet whether the responsible factor is prenatal or postnatal. He thinks that the evidence with regard to the part played by oxygen in the cause of this disease is contradictory and unconvincing.

Ingalls and Purshottam [20] note that similar, if not identical, ocular pathologic changes may be induced experimentally by antithetic disturbances of oxygenation, namely, either excessive amounts of oxygen or anoxia. They think that the rapid differentiation of the vascular network of the retina during the seventh and eighth months of fetal life is a determining factor in the development of retrolental fibroplasia but that additional factors are the erythrocyte count, concentration of hemoglobin, enzymatic and electrolytic patterns, body temperature, and humidity. An optimal supply of oxygen is necessary for normal development of the vascular system, but excessively high concentrations of oxygen initiate abnormal development of vessels in the premature retina through a mechanism not clearly understood as yet. Keeping the premature infant at adult body temperatures may be an additional factor.

After a comparative study of 105 prematures and 20 "immatures" (infants born after a 40-week gestation but weighing less than 5 lb.), Apple [21] concludes that prematurity of the infant and not its birth weight is the important factor leading to the development of retrolental fibroplasia. Interference with the normal process of retinal vascularization occurs apparently at the critical period between the 27th and the 32d week of gestation.

Krause [22] expresses doubt that administration of oxygen is a primary cause of retrolental fibroplasia. Thinking that edema and

vascular stasis might be caused by disturbance of water and electrolytic balance, he restricted the intake of salt to the amount in human breast milk and succeeded in reducing the incidence of retrolental fibroplasia so greatly that the condition developed in only one patient in each of the years 1950, 1951, and 1952. Wolfe [23] suggests that thyroidal dysfunction either in the mother or in the infant may be a factor in the development of the retinopathy of prematurity.

Francois and associates [24] think that their observations on the development of retinal lesions associated with chronic obstructive pulmonary emphysema help to explain the probable mechanism of retrolental fibroplasia. Of 20 patients who had pulmonary emphysema, they found the fundi normal in all but 1, who had mild edema at the poles of the discs resulting probably from secondary polycythemia. When patients who had cyanosis were given oxygen, the arteries became narrowed, the veins became dilated and more tortuous, mild edema developed in the macular regions, and capillary and flame-shaped hemorrhages appeared in the retina. The authors explain the retinal lesions on the basis of tissue hypoxia resulting from the arterial constriction caused by exposure to oxygen. In similar fashion, the retinopathy of prematurity developed, they think, if oxygen was given in concentrations greater than 30%. Retrolental fibroplasia did not develop in any of more than 200 prematures given 40% oxygen for two hours and then maintained on 25% oxygen even for several weeks.

Fletcher [25] states that eyes that are "mature" at birth tend to remain normal. However, about half of infants with birth weights less than 1500 gm. and the majority of those with birth weights less than 1250 gm. have "immature" fundi. These "immature" eyes undergo gradual transition to the "mature" type with normal adult vascularization of the retina. Some of the eyes, however, develop at this stage the hypervascular changes of early retrolental fibroplasia, which may regress after several weeks or may progress to the cicatricial stage of the disease. Fletcher states:

> From the observations reported herein, the disease, retrolental fibroplasia, appears to result from an as yet unknown factor or series of unknown factors affecting an immature eye which is passing through a period of critical differentiation and maturation.

Histologic Changes in Eyes of Infants.—Yoshioka [26] studied the eyes obtained at necropsy from 14 premature infants. In the retinas of 10 he found rosette formation, edema, hemorrhage, and proliferation of glial tissue and of the endothelium of vessels. The presence of degeneration in the fetal zone of the paranephros (adrenal) suggested a possible relationship between adrenal function and the development of retrolental fibroplasia.

Ward [27] examined 100 pairs of eyes of premature infants who were stillborn or who died shortly after birth to see whether or not histologic evidence might be present to suggest a congenital origin of or predisposition to retrolental fibroplasia. In 13% of the eyes he found an unusual degree of angioblastic activity indicated by the presence of increased amounts of vasoformative tissue in the nerve-fiber layer of the retina. This was associated with low birth weights and incomplete retinal vascularization but was not considered to be above the upper limit of normal. He did not find any nucleus of retrolental fibroplasia other than the incomplete retinal vasculature characteristic of prematurity.

Reese and Blodi [28] examined 122 pairs of eyes of infants who were stillborn or who died shortly after birth. They state that changes typical of retrolental fibroplasia may be present in a small percentage of cases. In 19 pairs of eyes, 12 of which were from premature infants, they found evidences of hematopoiesis in the choroid, vitreous, and orbit. This had not been recognized or described previously. They think that the haziness of the vitreous that has been described as an early sign of retrolental fibroplasia may be due to this hematopoiesis.

Experimental Studies.—Gyllensten and Hellström [29] studied the effects of adminis-

tration of approximately 100% oxygen to newborn mice. Continuous exposure to oxygen caused retarded formation of retinal vessels and proliferation of the hyaloid vessels. If oxygen was given continuously for five days and the mice were then transferred rapidly to a normal atmosphere and kept there for some days, progressive proliferation of the retinal vessels occurred, with capillary buddings into the vitreous, hemorrhages, and progressive foldings of the retina. However, these changes were accompanied by progressive proliferation of the hyaloid vessels; these latter changes were most striking if oxygen was administered intermittently or continuously without subsequent exposure to atmospheric air.

Ashton's group † reports further on their studies of administration of oxygen to newborn kittens. They state that high concentrations of oxygen at atmospheric pressure obliterate the ingrowing vessels in the developing retina of the kitten. This vaso-obliterative effect is influenced by the degree of maturity of the retinal vessels, by the duration of the exposure to hyperoxia, and by the concentration of oxygen. The vessels remain closed as long as the animal is kept in oxygen. On transferral to air, maximal vaso-obliteration is irreversible and revascularization of the retina commences from the margin of the disc, is abnormal and excessive, and extends into the vitreous. The vasoproliferation is controlled to a certain extent by return to hyperoxia. The vaso-obliteration is not prevented by the addition of 5% carbon dioxide to the oxygen or by the administration of tolazoline (Priscoline) hydrochloride, but ethyl biscoumacetate (Tromexan Ethyl Acetate) appears to prevent permanent vaso-obliteration, perhaps by preventing thrombotic occlusion of vessels that have been closed by spasm.

Patz ‡ again reports that the characteristic microscopic changes of human retrolental fibroplasia develop in newborn mice, rats, kittens, and puppies raised in a continuous high-oxygen atmosphere. In his opinion, rapid withdrawal from concentrated oxygen is not obligatory for the production of these lesions, although it may accentuate the injurious effect of continuous administration of oxygen.

Ashton and Cook [32] developed a limbal window technique that permits direct magnified observation and photography of the living retinal vessels in animals. Oxygen did not affect the retinal vessels of the adult cat. However, an immediate effect is noted on the developing retinal vessels in the kitten; within five minutes, the large vessels constrict and the capillaries are obliterated. After about 10 minutes the vessels dilate, but about 10½ hours later a delayed effect occurs; after about 8 hours more of continuous hyperoxia, the entire retinal circulation is completely obliterated. After this stage has been reached, the circulation may be either opened or closed in a period of five minutes by the alternate administration of air and oxygen. Vaso-obliteration cannot be induced in a detached retina.

In a study of the eyes of premature and full-term infants, of eyes with early retrolental fibroplasia, and of eyes from cats and rabbits, Serpell [33] found an intimate association of polysaccharide granules with developing retinal vessels and proliferating mesenchymal cells. These granules were proved to be glycogen. Their metabolic significance has not been determined as yet. Using the periodic acid-fuchsin stain, Patz § noted pronounced positive staining around the proliferating capillary buds in oxygen-treated animals.

RETINOPATHY IN DIABETES MELLITUS

Heinsius [34] thinks that pure diabetic retinopathy (capillary aneurysms, small hemorrhages, and small white spots in the retina) may be combined with arteriosclerotic lesions or venous changes or both in the retina. However, Ehlers [35] thinks that "simple" and "proliferating" diabetic retinopathy are two fundamentally different disorders and that it is not

† References 30 and 31.

‡ References 9 and 10.

§ References 9 and 10.

common for "simple" diabetic retinopathy to develop into the proliferative type. He presents a number of drawings illustrating various types of vascular and connective-tissue proliferation and calls special attention to accompanying rubeosis iridis, chorioretinal anastomoses, and production, through venous congestion, of a picture resembling choked disc. Hallum [36] reports development of bilateral papilledema in association with mild diabetic retinopathy in a 55-year-old man who had diabetes of 15 years' duration. The papilledema receded in about three months.

Incidence.—Howells [37] found retinopathy in 34 of 93 diabetic patients (37%); 67% of the patients with retinopathy had had diabetes for less than 10 years, 24% for 10 to 20 years, and 9% for more than 20 years. In examination of the eyes of 667 diabetics, Miratynska-Rusinowa and Lisiecka-Adamska [38] found aneurysms in 195 patients (29%), diabetic retinopathy in 129 (19%), and optic neuritis in 4. Nonnenmacher [39] reports that 129 of 614 diabetics (21%) hospitalized during the years 1950 through 1953 had retinopathy. He states that in younger patients retinopathy develops after 10 to 15 years of diabetes, whereas in older patients it is present after 5 to 10 years. He notes that 64% of all patients with retinopathy and 86% of the patients with the severer forms of retinopathy had hypertension. He thinks that the incidence of hypertension in diabetics had decreased during the years of subnutrition and had increased with improvement in nutrition.

Porstmann and Wiese [40] found that 326 of 720 diabetics (45.3%) examined during the years 1950 through 1952 had retinopathy; 12 (1.7%) had retinitis proliferans. The average duration of diabetes in the patients without retinopathy was 6.8 years, whereas in the patients with retinopathy it was 13 years. However, 83 of 315 patients (26%) with diabetes of less than five years' duration had retinopathy. They think that this unusually high incidence may be explained by delayed symptomatic manifestations of existing diabetes during World War II and the postwar years.

Relationship Between Retinopathy and Intercapillary Glomerulosclerosis. — Fontana [41] concludes from his studies that intercapillary glomerulosclerosis is instrumental in determining the appearance of diabetic retinopathy. Dana,[42] however, agrees with the more generally accepted view that both Kimmelstiel-Wilson disease and retinopathy are manifestations of a basic vascular disease. Using as the sole diagnostic criterion the presence of lumpy loops or hyaline masses in the glomeruli, he verified 57 cases of Kimmelstiel-Wilson disease. In 90% of these cases, extensive retinal aneurysms were found either ophthalmoscopically or in flat preparations of retinas obtained at necropsy. He thinks that the diabetes tended to become milder and acidosis rarely occurred after this syndrome appeared. Beardwood || does not agree with this last statement.

Sauer and Koch [43] note that, in spite of the fact that the age distribution and duration of diabetes are approximately the same in the various types of diabetic retinopathy, albuminuria is present in 75% to 80% of patients who have venous disease with or without proliferation and in only 15% of patients who have ordinary diabetic retinopathy. They think that the same pathogenic factors, as yet unknown, must account for the development of both proliferative retinopathy and glomerulosclerosis. They note that 20% of patients who had proliferative retinopathy died within three years, whereas only 3% of patients who had ordinary diabetic retinopathy died within such a period.

Pathogenesis.—In 165 patients with diabetes of 15 to 25 years' duration, Lundbaek [44] found retinopathy in 80%, nephropathy in 25%, occlusive vascular disease in the lower extremities in about 25%, and neuropathy in 5%. He thinks that these are manifestations of a specific diabetic vascular disease whose pathogenesis is unknown. Ditzel [45] states that modern hypotheses suggest that a metabolic

|| Beardwood, J. T., Jr., in discussion on Dana,[42] p. 211.

disorder of the simple polysaccharides (glycogen) or of the complex polysaccharides (mucopolysaccharides) involves the basement membrane of the capillaries, and impairment of the circulation in the terminal peripheral vascular system leads to prolonged suboxygenation and subnutrition of the endothelium. Nastri and d'Ermo [46] think that reduction in the protein content of the blood and increase in beta and gamma globulins may predispose to the development of retinopathy. Iannaccone and Kornerup [47] determined the plasma lipids in 100 diabetics and found the average values to be greater in the 41 with retinopathy than they were in the 59 without retinopathy.

Siliato [48] pancreatectomized eight dogs; four were given insulin and a lipotropic factor (anti-fatty-liver factor) and did not show any changes in the fundus in six weeks; in the other four, which were given only insulin, disseminated retinal hemorrhages appeared during the fourth week and gradually increased. He concludes that altered metabolism of fat is important in the pathogenesis of diabetic retinopathy.

Becker's group [49] reviews the evidence for excessive adrenal cortical function in diabetics with retinopathy and Kimmelstiel-Wilson disease and states that "it would appear that a vitamin B_{12} *deficiency* as well as *increased adrenal cortical activity* are involved in the pathogenesis of diabetic retinopathy and the Kimmelstiel-Wilson lesion." Becker and associates [50] elaborate further on this subject and suggest the possibility that a disordered metabolism of mucoids or lipoproteins may be a pathway of interaction between diabetes, vitamin B_{12} and the hormones of the adrenal cortex in the production of diabetic retinopathy and nephropathy.

Goodman [51] notes that retinopathy is associated with generalized increased capillary fragility or permeability. He states that the concept that retinopathy and glomerulosclerosis are caused not alone by lack of insulin but by the predominance of the pituitary hormones or cortical adrenal hormones or both, "though inviting, is still hypothetical and awaits confirmation."

Relation of Retinopathy to Control of Diabetes.—Landaburu and co-workers [52] state that retinal changes are more likely to occur in poorly treated patients than in those submitted to prompt, efficient treatment, adequate from the start and continued without intermissions. Beardwood and Trueman [53] think their findings in 385 unselected patients supported the view that rigid control of diabetes does reduce the incidence of retinopathy, especially of the severer grades. In 150 patients who had long-standing diabetes, Scott [54] found 62 (41%) with retinopathy. He could not demonstrate that control of the diabetes was a definite factor in the prevention of retinopathy, as the diabetes was considered to be uncontrolled in 30 of the patients with retinopathy and controlled in the remaining 32. However, 72% of the patients who had retinopathy were "defaulters" and came for check-ups only irregularly. Barach ¶ states that retinopathy may develop in well-controlled diabetes but it is likely to be less severe and destructive than it is when the disease is uncontrolled. Howells [37] apparently found a higher incidence of retinopathy in patients who had well-controlled diabetes than in those whose disease was not so well controlled. Yet he states that prevention of retinopathy is the most important and challenging problem in the management of diabetes and that it is foolish to ignore the importance of proper and adequate control of diabetes, particularly with regard to diet.

Treatment of Retinopathy of Diabetes.—Nonnenmacher [39] recommends the best possible care of diabetes so as to prevent variations in blood sugar if possible; he advises use of vitamins C, P, and K to combat bleeding tendencies and administration of sex hormones for their effect in inhibiting adrenocortical function. In addition to these measures, Heinsius [34] suggests use of calcium, vitamin E, and, if indicated in individual cases, vasodilators, anticoagulants, and resorptives. He states that progression can be controlled in 40% to 60% of cases. This appears to be a rather optimistic figure. Bottoni [55] tried

¶ Barach, J. H., in discussion on Dana.[42]

various types of treatment, including those just mentioned, in 115 patients; only 9 (7.8%) showed any improvement. Mehlhose [56] found specific retinal changes in 69 of 540 diabetics (13%). He treated them with rutin but did not obtain any predominantly positive results. He thinks that it might be worth while, however, for all diabetics, especially the young, to take rutin throughout their lives as a prophylactic against retinopathy. De Hoff and Ozazewski [57] gave alpha-tocopherol for 15 months to 12 patients who had diabetic retinopathy uncomplicated by hypertensive changes; it did not have any demonstrable effect on the progress of the retinopathy and did not improve vision.

Palmer and Waldman [58] think that further trial of combined treatment with male and female hormones is warranted. Nordlöw and associates [59] treated 15 males with male sex hormones and 12 females with various female hormones; improvement was noted in two patients who had severe retinopathies, one a man and one a woman. Becker and co-workers [59] state that a series of 20 patients with diabetic retinopathy treated with testosterone and vitamin B_{12} for more than nine months failed to show any improvement.

Luft and Olivecrona [60] state that they removed the pituitary gland from four patients with diabetes and retinopathy and from seven with malignant hypertension. They state:

> So far malignant hypertension seems not to be suitable for this operation, at least not until some form of pre-medication or some change in the technic makes it possible to avoid the ensuing acute cerebral edema. The same holds true for diabetes mellitus.

HYPERTENSIVE DISEASE

Ophthalmoscopic Changes.—By assigning weighted values to the various ophthalmoscopic signs of hypertension, Minsky # was able to construct a formula by which the severity of the hypertensive state could be appraised and an estimated diastolic pressure could be calculated. He thinks that an estimated pressure greater than the actual pressure indicates either a remission in the hypertensive disease or a decrease in blood pressure due to shock, closure of the coronary vessels, or myocardial failure; an estimated pressure less than the actual pressure suggests a psychogenic component in the increase of blood pressure.

Olmsted [63] calls attention to the different types of arteriosclerosis that occur in the eye and to their differential diagnostic features. He notes that the one definitely diagnostic sign of atherosclerosis is the visible atherosclerotic plaque and that, although the development of edema of the retina and optic disc is generally considered to indicate transition from the benign to the malignant phase of essential hypertension, spontaneous remission may still occur. Dehe [64] describes and pictures various types of arteriovenous crossing phenomena observed in 311 patients who had hypertension and 58 who had arteriosclerosis of the senile type. In his opinion, the crossing phenomena result from proliferation of the common adventitia of the artery and vein at the point of crossing and not from pressure of the artery on the underlying vein.

Wilson [65] discusses the significance of retinal lesions in hypertensive disease and expresses the opinion that papilledema in patients who have hypertensive retinopathy is most frequently evidence of the increased intracranial pressure that accompanies hypertensive encephalopathy. However, Taylor and co-workers [66] state that papilledema, increased pressure of the cerebrospinal fluid, and encephalopathy are to be regarded as specific, but as yet unexplained, manifestations of hypertensive disease, unrelated as to cause and effect. They checked the pressure of cerebrospinal fluid of 200 patients with hypertension; 87 of 100 patients with essential hypertension without papilledema and 57 of 100 with papilledema had cerebrospinal fluid under normal pressure.

Hypertension in Toxemia of Pregnancy.—Chesley [67] states that vascular constriction appears not to be a primary factor in preeclampsia and eclampsia, as other abnormalities typical of the syndrome often precede it. Finnerty [68] notes that true toxemia of preg-

References 61 and 62.

nancy can be differentiated from hypertensive vascular disease in a pregnant woman by examination of the ocular fundi. Characteristic of true toxemia is superficial edema of the retina (retinal "sheen") in association with retinal vessels that are normal except for segmental arteriolar spasm. Retinal arteriolosclerosis of the hypertensive type alone indicates hypertensive vascular disease that has preceded pregnancy. If retinal "sheen" is associated with hypertensive arteriolosclerosis, toxemia is superimposed on hypertensive vascular disease. Residual permanent vascular damage was found in 20 of 45 patients who had had true toxemia of pregnancy.

In a woman in whom severe acute hypertensive retinopathy had appeared during the eighth month of pregnancy, Meisner and Unger [69] found at necropsy a pheochromocytoma, neurofibromas in the skin, and cellular fibromas in the iris.

Coarctation of the Aorta.—Bonnet [70] expresses the opinion that the tortuosity of the retinal vessels seen in association with coarctation of the aorta is not caused by the hypertension but is a congenital anomaly, as it may involve the arteries or the veins or both and is not changed after surgical correction of the coarctation. He found tortuosity in 12 of 24 cases. Arteriolar narrowing, focal constriction, and sclerosis caused by the hypertension may be superimposed on the congenital tortuosity. Bonnet found a single hemorrhage in the retina in two cases.

Treatment of Hypertension.—A number of articles on the treatment of hypertension with various of the newer drugs have made reference to associated retinal lesions. Favorable response to treatment as evidenced by recession of the retinal lesions has been reported by Gifford and associates,[71] by Herbeuval and co-workers,* by Livesay and associates,[74] by Moyer's group,[75] and by Smirk.[76] However, Hughes and co-workers [77] report that, while 70% of 17 patients who had Group 1 hypertension responded well to treatment with reserpine (Serpasil), only 27% of 11 patients with Group 3 hypertension responded to such treatment. Herbst [78] states that the retinal lesions were improved by treatment with three hydrogenated ergot alkaloids (Hydergine) in two-thirds of patients who had "red" hypertension but in only 2 of 10 patients who were in the transitional stage from "red" to "pale" hypertension or who had well-developed angiospastic retinopathy. Shapiro and Grollman [79] state that hospitalized patients treated with hydralazine alone or with hydralazine and hexamethonium showed only infrequent and transient decreases in blood pressure directly induced by the drugs in doses that could be tolerated. Such clinical improvement as was noted, including regression of the retinopathy, was not always correlated with observed depression of the blood pressure.

Grob and Langford [80] report that during oral treatment with hexamethonium, retinopathy receded in two of seven patients, papilledema receded in three of seven patients and vision was improved in one of six. Under treatment with hexamethonium and hydralazine (Apresoline), retinopathy receded in seven of nine patients, papilledema receded in two of four patients, and vision improved in two of four. Among 30 patients treated orally with hexamethonium, dilated pupils developed in 5 and blurred near vision in 7. Among 24 patients treated with hydralazine (Apresoline), 4 experienced conjunctivitis, lacrimation, photophobia, and periorbital edema. In two patients who had malignant hypertension, reduction of blood pressure to normal or nearly normal levels was accompanied by transient loss of vision due to reduced blood flow to the retina.

Hypertension in Unilateral Renal Disease.—Howard's group [81] reports on six patients who demonstrated that hypertension in man can be produced by unilateral renal ischemia and can be cured by nephrectomy. Hypertensive retinopathy was present in four of the six patients; in two there was associated papilledema. The retinopathy receded completely in three patients after nephrectomy and was receding in the other patient at the

* References 72 and 73.

time of the last examination. The fundi were normal in one patient and showed only arteriolosclerosis in one.

Schaffer and Markowitz [82] analyze the results obtained in the treatment of hypertension by unilateral nephrectomy in 127 patients, including 4 of their own. Blood pressure was reduced in 28 of 30 children, the reduction being to normotensive levels in 20. Blood pressure was reduced in 56 of 97 adults, with reduction to normotensive levels in 41. Increase in caliber of the retinal arteries and disappearance of papilledema and retinopathy have been observed repeatedly, they state; however, the presence or absence of changes in the eyegrounds before nephrectomy appeared to have little bearing on the outcome.

Adrenalectomy in Hypertensive Disease.—Bowers [83] reports the results obtained after bilateral adrenalectomy in the treatment of 27 patients who had severe hypertension, including 11 who had malignant hypertension. He states that the blood pressure was decreased to normal levels in 20 of the 21 patients who survived the operation; the retinal lesions improved, and in one patient, particularly, vision improved remarkably.

RETINAL ARTERIAL AND ARTERIOLAR OCCLUSION

Presto [84] reports bilateral blindness with the ophthalmoscopic picture of ischemic edema of the retina resulting apparently from a postoperative decrease in blood pressure to levels concomitant with shock. Vision was not regained in spite of treatment with papaverine, tolazoline (Priscoline), and block of the stellate ganglion. Perese and co-workers [85] report a case of unilateral partial closure of the central artery of the retina that occurred during arteriography employing iodopyracet (Diodrast). Areas of ischemic edema were present in the retina and three plugs were visible in branch arterioles. Central vision gradually returned to normal but contraction of the visual field persisted. Wittich [86] describes a case of juxtapapillary chorioretinitis complicated by closure of a cilioretinal artery that he thinks was caused by edema and exudation in the surrounding retina.

Results of Treatment.—Remler [87] gave Hydergine to five patients who had closure of the central artery associated with hypertension; vision was not improved. Some improvement in the visual fields was noted in one case of closure of the central artery and in three of closure of branch arterioles that occurred in younger persons who did not have hypertension. Payne and Reed [88] traced the records of 73 patients who had retinal arterial occlusion, 22 of whom had been treated by the retrobulbar injection of acetylcholine. They state that treatment is of questionable value, as improvement in vision was recorded in only 1 of the 73 patients. Ocular palsies followed the retrobulbar injection of acetylcholine in five patients; the authors think that these complications were caused by action of the acetylcholine itself, and not by trauma from the needle.

Guillette and Mayer [89] report the successful treatment of a patient who had thrombosis of the central artery in whom they were able to start treatment within 40 minutes of the onset of loss of vision. Emergency treatment consisted of the inhalation of amyl nitrite, retrobulbar block with procaine, and intravenous injection of papaverine. Administration of heparin and bishydroxycoumarin (Dicumarol) was started about one and three-fourths hours after the onset, and use of anticoagulants, nicotinic acid, and sedatives was continued for six days. Administration of nicotinic acid was then continued for about six weeks, at which time the vision and visual fields were normal.

OCCLUSION OF RETINAL VEINS

Ennema and Zeeman [90] prefer the term "venous occlusion" to "venous thrombosis," as they think that true thrombosis is rarely encountered except in association with inflammatory or infectious processes. The intimate relation of the site of occlusion with structural peculiarities at arteriovenous crossings and at the lamina cribrosa suggests that the immediate cause of occlusion may

be mechanical. Occlusion of the trunk of the central vein has all the characteristics of simple persistence of the physiologic collapse of the vein. Inability of the vein to reopen might be due to decreased inflow of blood through an organically narrowed central artery, to an increase in intraocular tension, or to functional circulatory stasis. They note that vision was rather good in 19 of 36 private patients who had occlusion of branch vessels but was less than 3/60 in 19 of 22 patients who had occlusion of the central vein. However, 19 of 77 persons (25%) who had occlusion of the central vein seen in the outpatient clinic had fair vision. Wiedersheim [91] reports two cases of thrombosis of the central vein in patients who had hypertension and arteriosclerosis in which he thinks the precipitating cause was physical overexertion and local trauma to the orbital region.

Lister and Zwink [92] describe four types of anatomic end-results of occlusion of the central or tributary veins, namely, minimal formation of new vessels with probable recanalization, efficient by-passing of the occluded portion of the vein, inefficient replacement of the occluded vein by numerous fine new channels, and retinitis proliferans. They state that 4 of 12 patients (33%) who had thrombosis of the central vein and 8 of 13 patients (62%) who had thrombosis of a tributary vein recovered 6/12 or better vision.

Treatment of Venous Occlusion.—Dorello [93] noted definite improvement in vision, visual fields, and ophthalmoscopic appearance in six of seven patients who had thrombosis of the central or a branch vein treated with ethyl biscoumacetate (Tromexan Ethyl Acetate). Remler [87] stated that one patient with thrombosis of the central vein and two with thrombosis of a branch vein made good recoveries under treatment with Hydergine but that the recovery was not more rapid than with other methods of treatment.

The value and advisability of treatment of retinal venous occlusion with trypsin are as yet unsettled. Siliato [94] reports that intravenous injection of a fibrolytic enzyme of pancreatic origin had no effect in four patients who had long-standing thrombosis of the central vein; however, in four other patients in whom treatment was started immediately after the onset, recanalization of the vein and regression of edema and hemorrhage were observed. In a patient with thrombosis of the central vein treated with intravenous injections of trypsin for five days, Hopen [95] noted slight improvement in vision but no significant change in the fundus.

Clifton [96] states that use of trypsin in thrombophlebitis and related conditions is still controversial. Peck [97] said:

> A great deal more study needs to be done before this drug can be freely used in the treatment of patients. It may be that the dangers and reactions associated with trypsin will seriously limit the use of this particular enzyme when it is administered intravenously.

Taylor and associates [98] state that neither large nor small amounts of trypsin administered intravenously have any effect on artificially induced intravascular thrombi. Because of the dangers associated with its administration in sufficiently large doses to produce measurable effects on the mechanism of blood clotting, the use of trypsin for therapeutic purposes in man is not justified.

Fisher and Wilensky [99] state that, because of the untoward reactions from intravenously administered trypsin, they have discontinued its use. However, they have not noted any local or constitutional reactions from trypsin given intramuscularly, and they found that it had a definite tendency to shorten the course of acute thrombophlebitis. They do not mention treating any ocular conditions. Innerfield [100] records his observations, which indicate the safety of trypsin given intramuscularly over a long period. He thinks that, in addition to its acute anti-inflammatory effect in thrombophlebitis, it also has a salutary effect on the clot itself. Hopen and Campagna [101] obtained good results in the treatment of a variety of ocular lesions with trypsin given intramuscularly. They did not observe any untoward ocular or systemic reactions.

CRANIAL (TEMPORAL) ARTERITIS

Heptinstall and associates [102] report their observations on 14 patients who had temporal arteritis. One of their patients was only 48 years old, and one had diplopia. Seven had visual disturbances; two were blind in one eye, and two were blind in both eyes. In the 3 fatal cases, necropsy demonstrated widespread vascular changes affecting the aorta, the large arteries of the limbs, and the branches of the carotids. The histologic picture was distinctive, being similar to but not identical with that of polyarteritis nodosa. Arteritis was demonstrated histologically in both ophthalmic arteries in one of the cases of bilateral blindness, but the vessels were not completely occluded and the loss of vision was caused apparently by infarction of the occipital cortex on both sides. In another case, in which papilledema, hemorrhage, and exudate were seen ophthalmoscopically, histologic evidences of arteritis were not found in the ophthalmic or central retinal arteries.

Cordes [103] reports two cases of temporal arteritis and calls attention to the fact that the ocular symptoms in this syndrome may postdate by several weeks or months the time at which the temporal arteries are most acutely inflamed. Bässler [104] reports a case of bilateral blindness with the ophthalmoscopic picture of neuroretinopathy. Use of vasodilators and antibiotic therapy was of no avail. Siegert [105] thinks that ischemia of the optic nerve is caused by closure of small nutritive arteries of the optic nerve and not by obliteration of the central retinal or ophthalmic artery. He states that extirpation of the diseased temporal artery in cases with unilateral involvement is reliable prophylaxis against involvement of the other eye. However, Schirmer [106] states that a successful result from resection of the temporal artery is hardly to be expected beause of the peculiarities of the disease. He reports a case of bilateral blindness with the ophthalmoscopic picture of optic neuritis in one eye and occlusion of the central artery in the other.

Bonnet [107] calls attention to the fact that sudden permanent loss of vision associated with temporal arteritis may be preceded by episodes of amaurosis fugax. As long as the erythrocytic sedimentation rate remains increased, the disease is not cured and there is danger of ocular changes. He thinks that involvement of the central retinal artery is a part of the general arterial disease and not an extension from the lesion in the temporal artery. He states that limitation of ocular rotation might be caused by involvement of either the muscles themselves or their nerve supply. He advises biopsy of a temporal artery in all cases of sudden loss of vision in elderly persons. He considers administration of cortisone and corticotropin the treatment of choice for temporal arteritis, but he states that these agents do not prevent ocular complications and do not restore lost vision. Krysta [108] agrees with this opinion. On the other hand, Chapin and Frost [109] think that use of cortisone is effective in causing remission of the arteritis and in preventing complications and damaging sequelae.

Meyerratken [110] reports two cases of bilateral blindness of sudden onset due to ischemia of the optic nerves. Biopsy of the temporal artery revealed the typical changes of temporal arteritis in one case, but only obliterative endarteritis was found in the other.

CHORIORETINITIS IN TOXOPLASMOSIS

Congenital Toxoplasmosis.—Kimura and co-workers [111] observed 47 cases of uveitis in children less than 16 years of age. Posterior uveitis (chorioretinitis) was present in 29, and a presumptive diagnosis of toxoplasmosis was made in 10 of these; roentgenograms of the head were positive in 8 patients. Cases of chorioretinitis in congenital toxoplasmosis are reported by Long,[112] Masters,[113] Hill,[114] Lavat,[115] and Glees.[116] Toxoplasma cysts were found in the brain in one of Lavat's cases. Toxoplasma pseudocysts were demonstrated in the frontal lobe of Glees's case, and small structures were found in the retina that resembled pseudocysts but were too small for definite identification.

Toxoplasmic Chorioretinitis in Adults.—Jacobs and associates [117] did serologic tests

on 21 adult patients in whom the diagnosis of toxoplasmic chorioretinitis had been established by the finding of the specific organisms in the retinal tissues on histologic examination. Results of the dye test for toxoplasmosis using methylene blue were positive in all patients, but in varying antibody titers. The authors conclude that the only result of this dye test that can be considered definitely significant from a diagnostic standpoint is a completely negative one, as a titer of 1:256, for instance, is no more definitely diagnostic than a lower one.

A number of authors discuss the clinical and serologic diagnosis of ocular toxoplasmosis in the adult; among them are Woods's group,† Ashton,‡ Hogan,§ Hudson,‖ Fair,[122] Cathie,¶ and Smith.[123] The consensus appears to be that an increasing titer is more significant in diagnosis than the result of any single test. However, Woods and his associates, as well as Hudson, list titers that they consider significant for patients of different ages; in persons more than 20 years of age, they think the titer should be more than 1:64 to be significant. Woods's group state that titers obtained in dye tests were less than 1:256 in 90% of "normals" more than 20 years of age. They think that it is necessary to establish significant values for titers because, from a practical standpoint, the average ophthalmologist must base his evaluation of an individual case on the results of a single dye test.

Smith[123] expresses the opinion that the organisms of toxoplasmosis invade the retina initially, as noted by Ashton,# and that the resultant lesions are found in the posterior segment only. In more than 100 cases of active anterior uveitis, he found only the same evidences of Toxoplasma antibodies as would be present in healthy persons of similar age groups. Woods and his associates conclude from their survey that infection with Toxoplasma is the probable etiologic factor in approximately 25% of cases of adult granulomatous uveitis. The most frequent lesion is "focal" choroiditis; however, 10 cases of generalized granulomatous uveitis and 5 cases of retinal periphlebitis with secondary hemorrhage into the vitreous were noted among the 58 presumptive cases of toxoplasmosis. This disease was the possible cause also in two cases of optic neuritis. These authors state that there appears to be a 20% to 25% margin of error in the interpretation of results of a single dye test as an index of the possible presence of toxoplasmosis. On the basis apparently of a single dye test resulting in a titer of 1:64, Carreras Duran[124] ascribes to toxoplasmosis a case of retinal periphlebitis associated with abnormality of the plasma proteins.

The reports by Jacobs and associates* are of particular interest and significance. A 30-year-old man had had recurrent chorioretinitis in one eye for 8½ years. The eye was blind and painful and was enucleated. Pseudocysts containing spherical forms of Toxoplasma were present in the necrotic part of the retina and in the adjacent choroid. The identity of these parasites as living Toxoplasma gondii was established by serologic and cross-immunity tests after cultures and animal inoculations.

For the treatment of toxoplasmosis, Eyles[127] recommends sulfonamides, particularly sulfadiazine or its closely related compounds sulfamethazine (sulfamezathine) and sulfamerazine, in combination with the maximal safe dose of pyrimethamine (Daraprim). Beverley and co-workers[128] obtained complete or almost complete cures of experimentally produced toxoplasmic iritis in rabbits by treatment with a combination of 4,4′-diaminodiphenylsulfone and cortisone.

† References 118 and 119.

‡ Ashton, N., in discussion on Woods and others,[119] pp. 190-192.

§ Hogan, M. J., in discussion on Woods and others,[119] pp. 188-190; in discussion on Jacobs and others,[117] pp. 198-199.

‖ References 120 and 121.

¶ Cathie, I. A. B., in discussion on Hudson,[121] p. 488.

Ashton, N., in discussion on Woods and others.[119]

* References 125 and 126.

They suggest a trial of this combination in the treatment of human ocular toxoplasmosis.

THE RETINA IN VARIOUS SYSTEMIC DISEASES

Tuberculosis.—Saggese [129] states that lesions of the optic nerve are four times as frequent as choroidal tubercles in children who have tuberculous meningitis and that fundal lesions are less frequent in cases of isolated meningitis than in those associated with miliary tuberculosis. The lesions of the optic nerve vary from simple hyperemia or congestion to frank papilledema. Rarely, optic atrophy develops. Both the neural lesions and the choroidal tubercles tend to regress under treatment with streptomycin. Obal [130] thinks that, in some instances, edema of the optic discs, especially if less than 2 D., is indicative of optic perineuritis rather than of choking of the discs, and that optic atrophy is a typical finding in the late stages of tuberculous meningitis. He states that choked discs may recede under combined treatment with streptomycin and isoniazid.

Cremer and Cremer [131] report that results of the Middlebrook-Dubos test were positive in seven of nine cases of retinal periphlebitis that was thought clinically to be tuberculous. Juszkowa [132] treated 12 patients who had tuberculous chorioretinitis with retrobulbar injections of streptomycin and obtained good results.

Schlaegel and Hungerford [133] conclude from their studies that isoniazid is of value in the treatment of tuberculous uveitis but that it should be used in conjunction with other antituberculotic measures, such as administration of streptomycin, dihydrostreptomycin, and paraaminosalicylic acid, desensitization with tuberculin, and rest. Woods and associates [134] also recommend the combined use of isoniazid, streptomycin, and some adjuvant, such as paraaminosalicylic acid or thiazolsulfone. Woods [135] states, "It is almost certain that all clinical tuberculous disease of the eye is the result of an actual invasion of the ocular tissues by the Myco. tuberculosis in living form" and says that tissue sensitivity and acquired resistance largely determine the different clinical pictures resulting from this invasion. Treatment should include, he says, measures to increase resistance, to remove tissue hypersensitivity (tuberculin desensitization), and to attack the invading bacilli by bacteriostatic and bactericidal agents. Cortisone and corticotropin should be used only to control acute allergic reactions, and their administration should be discontinued as soon as these subside.

Pajtás [136] succeeded in arresting the course of the disease in six of eight cases of tuberculous retinal periphlebitis by the use of perforating electrocoagulation, along with streptomycin and paraaminosalicylic acid. Franceschetti and Forni [137] used surface diathermic coagulation over the areas of recent periphlebitis and newly formed vessels in 11 cases of recurrent retinal and vitreous hemorrhage in young persons; encouraging results were obtained.

Brucellosis.—Foggitt [138] reports a case of acute anterior uveitis in which results of intradermal and agglutination tests were positive for brucellosis. The uveitis subsided in about a month, but acute periphlebitis of the superior temporal vein with hemorrhage in the retina developed three weeks later in the other eye. Residual complete occlusion of the vein was present.

Infectious Mononucleosis.—Tanner [139] lists the various ocular manifestations of infectious mononucleosis and reports a case with edema of the optic discs that he thinks was due to papillitis or optic neuritis, although the vision was not much reduced. The edema receded in about two months.

Disseminated Lupus Erythematosus.—Brihaye-van Geertruyden and associates [140] describe recurrent cotton-wool patches in a case of fatal disseminated lupus erythematosus; the appearance and disappearance of these patches paralleled the gravity of the systemic condition. Histologically, cytoid bodies were found in the retina, and infiltration of mononuclear cells was present in the choroid. Tumulty [141] states that cotton-wool patches were present in almost 25% of his cases of systemic lupus erythematosus.

Ophthalmomyiasis.—Kiel [142] reports a case in which the larva of a fly migrated from the anterior chamber into the vitreous, with resultant massive bleeding into the retina and vitreous, followed by the development of an abscess in the vitreous that necessitated enucleation of the eye. Kiel thinks that larvae may enter the vitreous through the sclera and migrate into the anterior chamber. This may have been the course of events in the case reported by Galewska.[143] However, Hartmann [144] thinks that the concept that the larva usually enters the vitreous first and later migrates into the anterior chamber is contradicted by the favorable prognosis in cases of anterior ophthalmomyiasis (iridocyclitis) and the unfavorable prognosis in posterior involvement when larvae are present in the vitreous or subretinally.

Blood Dyscrasias.—On the basis of their observations in 42 cases of acute leukemia in children, Sansone and Mariotti [145] state that retinopathy is extremely frequent in this disease, associated usually with hemorrhage in other tissues and always with a decrease in platelets and a diminution in the number of megakaryocytes in the bone marrow. Eleven eyes were examined histologically; the typical changes were leukemic infiltration of the choroid, edematous or hemorrhagic infiltration of the retina, and optic neuritis with proliferation of neuroglia.

Henry and Chapman [146] found retinal lesions that they interpreted as manifestations of Eales's disease in 5 of 10 cases of sickle cell anemia and in 4 of 19 cases in which the sickle cell trait was present. They think that the lesions resulted from capillary infarction caused by impaction of the rigid and inflexible sickle cells.

Rudd and co-workers [147] observed hemorrhagic and exudative lesions in the retina in a case of thalassemia minor (hereditary Mediterranean anemia).

Cagianut and Hoffmann-Egg [148] state that the type of macroglobulinemia which is associated with severe disturbances of the central nervous system is characterized by typical changes in the fundus, exudative detachment of the retina with hemorrhage, and, at times, white patches in the retina and engorged veins that are irregular in caliber. Berneaud-Kötz and Jahnke [149] suggest the name "fundus paraproteinaemicus" to designate the type of retinal lesions caused by changes in the serum proteins. They describe a case with engorged cyanotic retinal veins with sausage-like constrictions, numerous zones of hemorrhage in the retina, and edema of the discs and of the peripapillary and macular portions of the retina.

Degeneration of Elastic Tissue.—Farnarier and Sobrepère [150] express the opinion that angioid streaks represent a degeneration of the lamina vitrea of the choroid associated with disciform degeneration of the macula, degeneration of the elastic tissue of the skin (pseudoxanthoma elasticum), and degeneration of the media of the arteries with possible widespread involvement of the cardiovascular system. François and Verriest [151] think that angioid streaks and the associated choroidal and retinal lesions represent a tapetoretinal degeneration localized at the posterior pole. In Cowper's [152] opinion, angioid streaks are excessively pigmented vessels in the choroid. He states:

> A weakness of the choroidal circulation with, at first, serous and, later, hemorrhagic extravasations, usually accompanied by migration of pigment epithelium to the affected vessels, would seem best to account for the streaks, as well as the associated fundus pathology.

Bossu and Lambrechts [153] found recurrent hemorrhages into the retina with unilateral retinitis proliferans in one of two cases of Ehlers-Danlos syndrome (hyperelasticity of the skin, hyperlaxity of the ligaments, cutaneous fragility, and a bleeding tendency, spontaneous or with even minimal trauma).

Pietruschka [154] found Junius-Kuhnt disciform degeneration of the macula in an 80-year-old woman who had Paget's disease of bone (osteitis deformans) but who had severe generalized arteriosclerosis also. He thinks that there is no direct connection between Paget's disease and angioid streaks, disciform or senile degeneration of the macula, or pseudoglaucoma; there is only a

chance association, age and arteriosclerosis being the factors common to these different conditions.

Trauma to the Thorax.—Kehler [155] describes severe edema of the retina with extensive hemorrhage and subsequently progressive optic atrophy in a girl who had been run over by a truck but who did not have an injury to the head or traumatic asphyxia. He thinks that fat embolism was probably responsible for the retinal lesions, although trophic degeneration resulting from acute venous stasis and impaired circulation was a possible factor. He found reports of 56 cases of trauma to the thorax in which visual disturbances were present. Retinal hemorrhage and exudates were present in 30 of these cases; optic atrophy was noted in 26, being unilateral in 12 and bilateral in 14. Traumatic asphyxia occurred in 27 of the 56 cases.

Air Embolism.—Thomas and associates [156] report two cases of temporary loss of vision that occurred immediately after injections were made into pleural cavities. The loss of vision was caused by ischemia of the optic nerve and retina in one case and probably by ischemia of the occipital cortex in the other. They think that the ischemia was caused by either direct lodgment of mixed blood and air emboli or spasm distal to the lodgment of an embolus.

Löffler's Syndrome.—Velzeboer [157] found chorioretinitis of the Jensen type in one eye and a lesion of the optic nerve in the other eye of a patient who had Löffler's syndrome (transitory pulmonary infiltration with eosinophilia).

Multiple Sclerosis.—Haarr [158] found retinal periphlebitis (perivenous sheathing) in 22.8% of 303 cases of multiple sclerosis; it was active in 9.2% and arrested in 13.6%. The active phase is seen most commonly during the first 10 years of the disease. A similar periphlebitis may cause the plaques in the central nervous system.

Raynaud's Disease.—In a woman who had Raynaud's disease, Vanni and Frugoni [159] found papilledema in one eye and secondary optic atrophy in the other, together with defects in the visual fields that they thought were due to vasospasm. Bilateral cervical sympathectomy was done, with resultant remarkable improvement in the function of each eye.

Pulseless Disease.—Caccamise and Okuda,[160] as well as Pinkham,† describe the ocular lesions in Takayasu's disease, or pulseless disease, a condition occurring most frequently in young women in which the blood pressure is extremely low in the head and upper extremities as a result of arteritis, usually nonspecific, in the large arteries arising from the aortic arch. In the retina, there is a pronounced decrease of blood pressure in the central artery, with resultant fragmentation in the blood stream in the retinal vessels. Characteristically, progressive peripapillary and peripheral arteriovenous anastomoses are present, and permanent obliteration of the columns of blood in the peripheral vessels may occur. Hemorrhage may occur into the retina and vitreous, with retinitis proliferans. The deficiency of arterial blood supply results in chronic subnutrition of the eyes, and cataracts develop. However, the vision continues to fail progressively even if the cataracts are removed. Caccamise and Okuda present sketches of the retinal lesions in two typical cases. Pinkham reports a case in a 32-year-old Negro woman. He noted the characteristic subjective symptoms of intermittent blurring of vision and severe reduction of vision when the patient stands or looks up. Jervell [161] reports a case of pulseless disease of 13 years' duration in which the optic discs and retinal vessels appeared normal; scattered punctate and somewhat larger red spots, either hemorrhagic spots or small aneurysms, were seen in the retina, especially at the periphery. Ashton [162] called attention to the similarity between the retinal picture in the late stages of pulseless disease and the neovasculariza-

† Pinkham, R. A.: Ocular Manifestations of the Pulseless Syndrome, read at the 17th International Congress of Ophthalmology, New York, Sept. 12-17, 1954.

tion produced by exposure of newborn kittens to high concentrations of oxygen; the neovascularization in both conditions is due to severe retinal anoxia.

Loss of Vision Resulting from Anoxia.—Givner [163] reports a case of cardiac arrest with temporary loss of vision that he ascribes to edema of the occipital cortex rather than to local retinal pathologic changes.

Duane [164] determined by ophthalmoscopic observation during black-out that the loss of vision is due to local retinal ischemic anoxia.

Associated Retinal and Cerebral Lesions.—Huber [165] discusses the relationship between the retinal and the cerebral vessels. He notes that arteriolosclerosis of the hypertensive type in the retina indicates the presence of similar lesions in the brain and kidneys; atherosclerosis may be confined to one location. If the retinal diastolic pressure decreases to less than 25 gm. after ligation of the carotid artery, he thinks that vascular insufficiency will develop on that side of the brain. A difference in the retinal diastolic pressures on the two sides is rarely found in suspected cases of chronic thrombosis of the internal carotid but is suggestively diagnostic if present.

Hemangiomatosis.—Silver [166] accumulated information on 96 descendants in seven generations of a family started in Virginia in 1788. The presence of vascular tumors was verified in 19 of 61 members of this family and was suspected from symptoms in an additional 8. He states that the diagnosis of familial hemangiomatosis depends on the demonstration of two such vascular lesions in the same patient or the demonstration of a single lesion in a patient with a verified family history. Study of pathologic specimens from patients with vascular tumors of the nervous system indicates uniformity of the lesion regardless of whether its location is in the retina, cerebellum, or spinal cord; the tumors are capillary cavernous hemangiomas and often are associated with cysts. Irradiation has not been demonstrated to control the growth of these tumors. Surgical coagulation apparently modifies the course of the lesion in the retina but rarely preserves useful vision. However, Kent [167] and Straatsma [168] each report diathermic coagulation of a retinal hemangioblastoma with preservation of good vision.

Sapuppo [169] found an angioma in the retina close to the optic disc in a patient who had Morgagni's syndrome (endocraniosis with frontal hyperostosis, obesity, hirsutism, arterial hypertension, and alterations of the cerebral venous system).

Piper [170] describes cavernous hemangiomas in the retinas of two children. He thinks that they developed from the capillaries or precapillaries and that they were not connected with the large retinal vessels. Associated systemic changes that might be expected in a phacomatosis were not present, and Piper thinks that the tumor-like formations were of inflammatory origin. Tuberculosis was suspected in one of the cases, as a pulmonary lesion was present.

Arteriovenous Aneurysms.—Riffenburgh [171] calls attention to the frequent association of arteriovenous aneurysms of the retina with similar lesions in the midbrain. In the case that he reports, however, the lesion in the retina did not change in appearance, and evidence of a neurologic lesion was not found during a nine-year period of observation. Glees [172] describes an arteriovenous aneurysm covering most of the right optic disc of an 11-year-old boy who had left homonymous hemianopsia, slight left hemiparesis, thickening and doughy swelling of the skin of the right cheek and right occiput, and a tumorous thickening of the mucous membrane of the right upper and lower jaws. An arteriogram demonstrated an arteriovenous aneurysm on the right side of the brain extending into the right orbit.

Subarachnoid Hemorrhage.—Manschot [173] reviews the clinical records of 225 patients who had spontaneous subarachnoid hemorrhage, all of whom had at least one ophthalmoscopic examination. Also, he studied histologically the globes and orbital portions of the optic nerves of three patients with intra-

ocular hemorrhage and the bony optic canals and surrounding tissues of three patients in whom there was hemorrhage between the sheaths of the optic nerves but in whom retinal hemorrhage had not been observed during life. Retinal hemorrhage was present in a fifth and papilledema in a sixth of the patients. He states that hemorrhage may be found in the retina within an hour after the onset of the intracranial hemorrhage and that these hemorrhagic areas may be small, not necessarily subhyaloid. The degree of papilledema is usually moderate; the discs are "blurred" or "lightly swollen." Manschot states that he demonstrated an open communication between the subarachnoid space of the brain and that of the optic nerve in the orbit. The passage of blood through this open communication can occur with such force that intradural hemorrhage occurs as a result of rupture of the inner layers of the dura. The central retinal vein and its choroidal anastomoses are closed by the high pressure; the resultant back-pressure into the retinal veins causes ruptures in the veins and bleeding into the retina. Hemorrhage into the orbit and into the intracranial portion of the optic nerve, the chiasm, and tracts is explained by arterial overfilling and not by venous stasis. The infrequent occurrence of ocular involvement may be explained by the fact that, in many cases, the blood only oozes from the ruptured aneurysm. Manschot gives his reasons for disagreeing with Ballantyne ‡ and with Walsh and Hedges § on the mechanism of production of the hemorrhage in the retina and orbit.

RETINAL DETACHMENT

Ophthalmoscopic Appearance. — Stallard [174] reports six cases in which there was annular peripheral detachment of the retina without definite holes and with a rather dark color, suggesting inclusion of the choroid in the detachment. Both eyes were involved in three of the cases. Complete spontaneous replacement of the retina occurred in one eye and partial replacement in the other eye in a case of bilateral detachment. Successful operations were done in three cases by diathermic puncture. This type of detachment must be differentiated from ring sarcoma.

Agarwal [175] describes eight cases of double-balloon formation in detachment of the retina due to persistent adhesion between the inner and outer layers of the retina in the region of the fetal cleft. In two of the eight cases, a hole was present in the upper part of the retina. An anterior dialysis retinae was present behind each balloon in the other six cases. Rais and associates [176] report a case of lateroversion of the retina in a "high" myope that did not follow trauma and that was associated with an enormous tear in the temporal portion of the retina and not with an oral disinsertion.

Favre [177] states that when ophthalmoscopic examination fails to reveal a tear in detachment of the retina in myopic eyes, examination by means of the slit lamp may locate the hole, often quite small, in the peripapillary region associated with detachment of the vitreous at its posterior attachment around the optic disc. Simonelli and Faldi [178] describe and discuss the technique of intravenous injection of fluorescein sodium and Geigy blue for better visualization of retinal tears.

Pathogenesis and Etiology.—Mawas [179] expresses the opinion that retinal detachment cannot occur unless there is a lesion of the retinal pigmentary epithelium secondary to various disorders in the choroid. The diseased epithelium either permits transudation of fluid or actively secretes fluid that detaches the retina. The vitreous is not the primary factor in the development of the detachment but is involved secondarily because of loss of nutrition derived from the pigmentary epithelium. Holes or tears in the retina are produced by degeneration of the retina and not by traction from the vitreous. However, Arruga [180] doubts that the retinal pigmentary epithelium secretes subretinal fluid. He interprets retinal de-

‡ Ballantyne, A. J., cited by Manschot.[173]

§ Walsh, F. B., and Hedges, T. R., cited by Manschot.[173]

tachment as a mechanical accident. In the majority of cases, he states, the retina is atrophic and adherent to the framework of the vitreous. Retraction of this framework tears the retina in one place. Sometimes at the moment of a tear, a vessel is opened and bleeding into the vitreous occurs. During movements of the eye, the vitreous strikes the edges of the hole in the retina, enlarges it, and passes behind it. A tag of retina may become detached into the vitreous.

Massin [181] states that it is often difficult to evaluate the role of trauma, direct or indirect, in development of ordinary senile or myopic detachment of the retina. He states that contusion of a healthy globe does not cause immediate detachment of the retina but may cause Berlin's edema, which at times simulates detachment but which usually recedes rapidly, or a rupture of the choroid with retinal edema and hemorrhage into the retina and vitreous. Atrophic and proliferating chorioretinitis resulting from the primary rupture may be complicated later by detachment of the retina. Likewise, a penetrating wound with or without an intraocular foreign body may cause a late secondary but not an immediate detachment of the retina. Definite statistics are not available to show whether or not early diathermic coagulation of the scleroretinal wound will diminish the frequency of occurrence of this late detachment. A special type of detachment of the retina in young persons, a flat detachment of the inferior part of the retina with disinsertion, located usually in the lower temporal quadrant, appears to be post-traumatic in about a third of the cases. However, the basic cause is peripheral chorioretinitis or cystic disease of the retina, and the trauma is only an accessory factor.

Vannas and Voipio [182] report development of bilateral symmetrical detachment of the retina after persistent edema of the lower portion of the retina that may have been initiated by an attack of nephritis. Later, dialysis retinae was found in the lower temporal periphery of each eye.

Westsmith and Abernethy [183] describe development of a large bullous detachment of the temporal half of the retina of one eye during treatment of chronic glaucoma with isoflurophate (diisopropyl fluorophosphate; Floropryl). The retina became reattached after closure of the tear by diathermy. Low tension was maintained in the eye. The authors stated that a few similar cases had been reported previously.

Paycha [184] presents his observation in support of the idea that the tissue changes caused by deficiency of vitamin A predispose the eye to the development of retinal detachment, although such changes do not constitute an actual exciting cause. Stagni [185] noted that the tear in the retina was near the insertion of one of the extrinsic ocular muscles in 51 of 72 detachments. As a result of their experience in the experimental production of retinal detachment in the eyes of rabbits, Alajmo and Auricchio [186] suggest that hyaluronidase may play a part in the development of idiopathic detachment of the retina in man.

Surgical Procedures.—Dellaporta [187] describes a new method of endodiathermy for closing retinal tears in the posterior segment of the eye under direct ophthalmoscopic observation that is particularly applicable to the sealing of holes in the macula. Bonavolontà [188] studied the effects of diathermy on the retina in cases of retinal detachment. He noted that in 32 of 50 cases the retina was well away from the choroid at the time of operation; in the remaining 18 cases, the retina was approximated to the choroid. In this latter group, as compared with the former, the retina was visibly coagulated when diathermy was applied, the destructive effects on the retina were severer, and healing was slower. Bangerter [189] reports successful closure of macular holes by retrobulbar implantation of placental or amniotic tissue.

Scleral Resection: Koenig [190] states that lamellar resection or scleral buckling is a simpler and safer procedure than full-thickness scleral resection and is equally efficient. He thinks that it should be used as a primary procedure and not only as a last resort. Böhringer [191] agrees and points out that the operation is more difficult technically in a

previously coagulated area of the sclera. Dellaporta [192] found that an identical permanent shortening of the normal eye of a dog can be achieved by either full-thickness scleral resection or scleral folding. However, reattachment of the retina is more rapid and considerably firmer after scleral resection, because of significant inflammatory changes in the uvea and sclera.

Shapland [193] states that in all except highly myopic eyes the increase in hyperopia or decrease in myopia after lamellar scleral resection rarely has been greater than 2 D., and this change in refraction tends to diminish in the course of time. Postoperative astigmatism of 2½ to 3 D. usually remains permanently. The myopia was reduced 5½ D. in one highly myopic eye and 8 D. in another. After electrocoagulation of the holes in the detached retina, Lindner [194] shortened two highly myopic eyes 8 to 10 D. by complete circular resection of a strip of sclera 3 to 3.5 mm. in width in the equatorial region. He discusses the technical difficulties of this operation.

Results of Surgical Treatment: Frey [195] states that the retina was reattached in 126 of 197 eyes (64%) operated on for retinal detachment. Two operations were necessary on 42 eyes, three operations on 16 eyes, and four operations on 1 eye. Successful results were obtained in 64% of eyes treated by diathermic coagulation for closure of retinal tears, in 26% of those treated by full-thickness scleral resection, in 16% of those treated by lamellar scleral resection, in 53% of those treated by combined closure of tears and full-thickness scleral resection, and in 28% of those treated by combined closure of tears and lamellar scleral resection.

Kronfeld and Pischel [196] report that 62 (31%) of 200 full-thickness scleral resections for retinal detachment were successful and that 121 (60.5%) were failures. In the remaining 17 cases (8.5%), some improvement was noted but the retina was not reattached. The authors discuss the pathogenetic factors that influenced the success or failure of the operation.

Infante [197] obtained good results from lamellar scleral resection in four of seven patients who had extensive retinal detachment of long standing. Shapland [193] obtained successful reposition of the retina in 42 of 71 eyes (59%) subjected to lamellar scleral resection. He noted that in some eyes the detachment may subside gradually in the course of several months after apparent initial failure. The retina became reattached in 8 of 17 eyes in which Basterra [198] combined scleral resection and diathermy.

Rumpf [199] noted that successful results had been obtained in 60 of 96 eyes operated on for detachment of the retina. Reexamination was done 14 to 18 years after treatment with regard to 24 of these 60 eyes; the retina was in position in all. In 11 other cases, follow-up reports indicated that the retina was still attached.

Systemic Complications of Surgical Treatment: Scher [200] states that systemic complications occurred in 21 of 263 patients (8%) during the period of hospitalization after operation for retinal detachment. He lists these complications as vascular, cardiac, gastrointestinal, respiratory, urinary, and miscellaneous. One patient died. Scher does not think that any correlation existed between rest in bed and the occurrence of systemic complications.

TUMORS OF THE RETINA

Retinoblastoma.—Rintelen [201] thinks that it is not possible to predict from the histologic character of a retinoblastoma the future course of the disease or the probability of involvement of the other eye. He states that retinoblastomas do occur sporadically. Therefore, before the physician advises a person who has had a retinoblastoma whether or not to have children, the family history should be carefully investigated; the chance of a survivor transmitting a tendency for this tumor to descendants is much less if the family history is definitely negative.

Treatment.—Streiff [202] states that early enucleation is imperative in unilateral malignant tumors of the retina. Radiation therapy

or destruction by diathermy is indicated only if the tumor is present in a remaining eye or, in the case of bilateral tumors, when enucleation is refused or after enucleation of the more severely affected eye.

Stallard [203] treated 16 retinoblastomas in the years 1934 to 1948 by insertion of radon seeds and 21 between the years 1948 and 1952 by application of radium discs. Of the 36 patients involved (37 eyes), 28 kept some useful vision; 6 had 6/6 vision, and 2 had 6/9. There was no evidence of recurrence of the tumor in the irradiated eyes. Ten of these 28 patients were alive 5 to 18 years after the irradiation. Five of the irradiated eyes had to be enucleated because of retinal detachment, hemorrhage into the vitreous, or secondary glaucoma; in none was there any clear histologic evidence of active retinoblastoma cells. It was noted that small neoplasms (less than 5 mm. in diameter) might disappear within three or four weeks; the maximal effect on larger growths is attained in about two months.

In the histopathologic study of eight eyes containing irradiated retinoblastomas, Stallard found that the ultimate fate of irradiated blood vessels is attenuation and disappearance of all or part of the vascular tunics. These vascular changes play an important part in the disappearance of the neoplasm, and they are responsible also for such late complications as intraocular hemorrhage and radiation cataract. Stallard concludes from his studies that reasonable hope exists that a retinoblastoma may be destroyed by radiation therapy if it involves less than a third of the retina. With few exceptions, results will be bad if one-half or more of the retina is involved. A dose of 2500 to 3500 r at the summit of the neoplasm is usually effective. Irradiation fails when the choroid is infiltrated by the tumor. In Stallard's opinion, the most satisfactory method of treatment is the application of radium discs made to fit the curvature of the sclera, as the radiation can be applied close to the target quickly in a concentration that is effective and still is reasonably safe for the eye.

Dollfus [204] agrees with Streiff as to the indications for enucleation or radiation therapy of retinoblastomas. If the second eye is involved some time after enucleation of the first, he states that irradiation should be attempted only if the surface extent of the tumor is not greater than a third of the retina and the tumor is not more than 6 mm. in thickness. Also, it should not be situated exactly over the optic disc, as tumors in this location are prone to intracranial extension. In his experience, five-year cures have been obtained in 28.5% of the patients treated by surface application of radium and in 11.5% of the patients treated by roentgen rays. Surface application of radium by Stallard's method would appear to be the preferred treatment.

Radioactive Phosphorus in the Diagnosis of Intraocular Malignant Neoplasms.—A number of papers on this subject have been published recently. Dunphy and co-workers [205] continued the studies reported by Dunphy and Selverstone in 1953. They call attention to the fact that localization of malignant lesions by radioactive phosphorus (P^{32}) is possible only when the tumor is growing in a bed of metabolically slow-moving normal tissue. The eyeball meets this requirement because of the large volume of the globe occupied by the metabolically torpid sclera, aqueous, vitreous, cornea, and lens. The portion of the eye containing a malignant melanoma or a retinoblastoma was found to show an increased uptake of P^{32}; however, Dunphy's group thinks that, for practical diagnostic use of the method, some type of Geiger counter will have to be devised that can be applied behind the equator of the globe. Later in the year, Thomas and associates [206] described a Geiger-counter probe that they had found satisfactory for use in the study of lesions behind the equator in the extreme posterior portion of the globe. The probe was designed for insertion through an opening in the conjunctiva and Tenon's capsule against the sclera adjacent to the suspected tumor.

Bettman and Fellows [207] studied the uptake of P^{32} by the normal eyes of a group

of patients who had been given large amounts of this isotope for the treatment of polycythemia vera. They call attention to different factors that could cause variations in the count. They noted that inflammation causes a great increase in the counting rate and that the vascularity of a tumor influences the counting rate considerably. If the count is taken shortly after the intravenous injection of P^{32}, the rate may be less over an avascular tumor, such as a retinoblastoma, than over the normal eye. They suggest, therefore, that it might be well to let a longer interval elapse before taking the count.

Thomas and co-workers,[208] in a study of 44 intraocular lesions of various types, found that measurement of the differential uptake of P^{32} by tumors appears to indicate a clear separation of neoplastic from non-neoplastic disease. The test is not satisfactory unless the counter can be placed within 5 mm. of the probable location of the suspected tumor. They note that the differential does not show up until two or three days after the injection in cases of retinoblastoma. They state that the determination of uptake of P^{32} is an adjunct to careful clinical evaluation of suspected intraocular tumors and not a conclusive diagnostic test.

Eisenberg and associates [209] state that neoplasms in the anterior segment show a significant detectable concentration of P^{32} and that active inflammatory lesions do also. Lesions in the posterior segment may or may not do so, depending on their size, activity, and location. Serous detachment of the retina and hemorrhage in the choroid and vitreous do not show a significant concentration. A concentration more than 30% above the arithmetic mean of the counts in the normal eye is considered significant. In a subsequent publication, Eisenberg's group [210] state that the method of studying uptake of P^{32} that had been reported previously did not differentiate between inflammatory and neoplastic lesions, although it did differentiate these from serous detachment of the retina. The technique was changed, therefore, to include readings taken 1 hour after the injection and 24 hours later. To be positive for malignant lesions, results of the test must show a concentration of P^{32} in the suspected lesion at least 30% greater than the average in the normal eye, and the concentration at the end of 24 hours must be greater than that 1 hour after the injection. Results of this test were positive in all of 19 malignant melanomas of the choroid, in 2 of 4 retinoblastomas, in 1 metastatic carcinoma of the choroid, and in 2 malignant lesions of the iris. Results were negative in all of 34 cases of serous detachment of the retina, in all of 13 instances of inflammatory detachment, and in all of 10 hemorrhagic lesions. The test was decidedly less accurate in the diagnosis of retinoblastomas in children than it was in the diagnosis of other malignant lesions.

Town [211] notes that the differential diagnosis of a solid and a serous detachment of the retina is often difficult. Results of ophthalmoscopic examination may be inconclusive, and transillumination may give doubtful information. Tears in the retina are present in almost all instances of serous detachment, but the presence of a tear does not rule out a tumor. The intraocular tension is not always increased even if the tumor is large. In Town's experience, the use of radioactive phosphorus has proved of great value in the differential diagnosis. Results of the test were positive in 3 of 20 cases of retinal detachment; histopathologic examination confirmed the presence of a malignant tumor in all 3. Results of the test were negative in the remaining 17 cases; findings at operation, together with the subsequent course, confirmed the fact that serous detachment was present in these 17 cases.

RETINAL DEGENERATION

Stephenson [212] presents a classification, with notes on the pathology and modes of inheritance, of the hereditary retinal abiotrophies, including primary pigmentary degeneration of the retina, heredomacular degeneration, generalized macular dystrophy, maculocerebral degeneration, familial lipid

degeneration, gyrate atrophy of the choroid and retina, choroidal sclerosis, and congenital night blindness.

Strazzi [215] reports retinitis pigmentosa sine pigmento in two brothers, aged 7 and 13 years, who presented the syndrome of Bardet-Biedl (Laurence-Moon-Biedl syndrome). Typical retinitis pigmentosa had developed in the older brother five years later. Another patient, who had hypogenitalism on a diencephalic-hypophyseal basis, originally had hemeralopia (night blindness?) with a normal fundus; scotomas and pigmentary migration into the retina developed later.

Jager [214] describes an unusual type of macular degeneration, which he terms "central retinoschisis," in 26 patients, 25 of whom were members of six families. In half the patients, the macular lesions were associated with degeneration of the retina, usually peripheral in location, that simulated proliferative retinopathy. The degenerative process appeared to be hereditary and sex-linked; on histologic examination, it was found to involve the most superficial layers of the retina.

Rosehr [215] examined two sisters who had familial macular degeneration; his examination was done 50 years after these patients were seen first by Stargardt. In the older sister, 70 years of age, the area of degeneration in each eye, originally 1½ to 2 disc diameters in size, had progressed to involve the entire posterior pole between the superior and inferior temporal vessels from the margin of the disc to beyond the macula. Considerable atrophy of the choroid had developed, and pigmentary deposition had increased. The discs were pale, the retinal arterioles contracted, and accumulations of pigment were present in the periphery. In the younger sister, aged 63, the lesions had progressed relatively little. The optic discs were normal, with senile halos. The retinal vessels were normal. There was atrophy of the choriocapillaris, with visible large choroidal vessels and patchy collections of pigment in areas about 2½ disc diameters in size in the disc-macular regions. Rosehr classified the lesions as tapetoretinal degeneration.

Oksala [216] reports 12 cases of juvenile macular dystrophy. All patients were males who had rather rapidly developing, symmetrical macular lesions characterized by absence of the foveal reflex and the presence of a grayish, tree-like meshwork deep to the retinal vessels radiating from the fovea; these lesions occurred in an area of ½ to ¾ disc diameter in size without cysts or formation of holes and without pigmentary deposition. In 9 of the 12 cases, the lesions were known to have developed at the age of 7 to 9 years, and Oksala thinks that they may have been caused by growth factors, possibly the irregular increase in the volume of the globe.

Klien [217] studied the eyes of a 5-year-old boy who had had progressive paralysis, mental deficiency, and blindness since the age of 14 months. Ophthalmoscopic examination revealed grayish-white optic discs, only traces of retinal vessels, a mottled appearance of the fundi with some fine pigmentary deposition, and round, dark, punched-out foveas without reflex. Histologic examination of the eyes obtained at necropsy showed swelling and degeneration of the retinal ganglionic cells and complete destruction of the first retinal neuron, with proliferation and migration of pigmentary epithelial cells and replacement by a thick glial plate. The optic nerves were completely atrophic. The vessels in the optic nerve and retina were obliterated. The punched-out appearance of the foveas was found to have been caused by the abrupt ending of the gliotic retina at the edges of a slightly pigmented glial plate apparently derived from the pigmentary epithelium. Histologic examination of the brain revealed extreme atrophy with generalized degeneration of the ganglionic cells and compensatory proliferation of neuroglia. The case was classified as an example of late infantile amaurotic familial idiocy because cerebral lesions and lipid degeneration of the retinal ganglionic cells typical of the infantile type were combined with primary degenera-

tion of the first retinal neuron characteristic of the juvenile type.

THE OPTIC NERVE

Blood Supply.—François and Neetens [218] present an extensive survey of the blood supply of the optic nerves. As a result of their studies, they determined that the ophthalmic artery is not the only vessel that supplies the optic nerve. There are anastomoses with branches from the external carotid system that contribute to the nourishment of the optic nerve through the network of the pia-mater. The central retinal artery supplies only the retina, not the optic nerve. Early in its course the ophthalmic artery gives off a central artery to the optic nerve that supplies both the intracanalicular and the intra-orbital portion of the nerve. Anastomoses between capillaries from the circle of Zinn-Haller and the anterior ramifications of this central artery supply the head of the nerve. Capillaries from anastomoses between extra-orbital cerebral vessels run into the pial sheath and help to supply the optic nerve.

Congenital Defects.—Smith [219] reports on three patients who had so-called aplasia of the optic nerve; the condition was bilateral in one and unilateral in two. The optic discs were white and about a third of the normal size in the patient who had bilateral disease and in one of the patients who had unilateral disease; the disc was less than half-normal size in the other patient, who had unilateral disease. There was no visible differentiation of the macular area. Smith thinks that the term "hypoplasia" would be more accurate than "aplasia," as the optic disc and the retinal vessels should not be present in true aplasia. He did not find any associated neurologic disturbances in his cases.

Sweng [220] reports extreme unilateral proptosis in a newborn. When the eye was enucleated, a large cyst about four times the size of the globe was found in the orbit. It was attached by a 3-mm. pedicle to the optic nerve approximately 5 mm. behind the globe and proved to be of developmental neural origin, probably an anomaly of the developing optic vesicle.

Hereditary Optic Atrophy.—Jaeger [221] investigated cases of dominant hereditary optic atrophy in four families. In four generations of one of the families, 35 persons were affected; males and females were equally involved. Ophthalmoscopically there was simple optic atrophy characterized mainly by pallor of the temporal parts of the discs. Central visual acuity varied from $\frac{1}{60}$ to normal. The visual fields for white were usually normal; when the lesions were more advanced, the fields for white showed mild concentric contraction and enlargement of the physiologic blind spots. The fields for colors always were contracted, more so for blue than for red. A characteristic disturbance of color perception was always present, even when the central visual acuity was normal. Blue-yellow vision was affected more than red-green. Jaeger thinks that this type of involvement of the optic nerve begins in early life, is very slowly progressive, and seldom leads to invalidism.

From his observations in five cases of Leber's hereditary optic atrophy occurring in three generations of one family and from his review of the literature, Huerkamp [222] concludes that lesions of the retina are not rare in this disease. Affected persons may complain of chromatopsia and ring scotomas; edema, hemorrhage, pigmentation, and sheathing of vessels may be seen in the retina. These changes are thought to be analogous to the optochiasmatic arachnoiditis seen in association with involvement of the optic nerve.

Optic Neuritis.—Teuns [223] reports bilateral optic neuritis in a 10-year-old boy that improved after eight injections of cortisone followed by intramuscular injections of tolazoline hydrochloride. The boy had had bilateral epidemic parotitis 20 days before the onset of the neuritis. Mild pleocytosis was present; the cerebrospinal fluid was under normal pressure. The virus of mumps was isolated from the cerebrospinal fluid. Results of complement fixation tests on blood using mumps antigen were positive in high titer; results of the test on cerebro-

spinal fluid were negative at first but became positive later.

Tumors of the Optic Nerve.—Marshall [224] presents a rather extensive review of the subject of gliomas of the optic nerve, with particular emphasis on their relationship to Recklinghausen's disease (neurofibromatosis). Reports in the literature would suggest that between 20% and 30% of gliomas of the optic nerve and chiasm, which are usually astrocytomas, are manifestations of Recklinghausen's disease; the actual percentage is probably much greater, however. Marshall states that a primary tumor of the optic nerve in the orbit usually causes loss of vision, exophthalmos, and pallor of the disc; sometimes papilledema is present, and enlargement of the optic canal is produced if the tumor extends into it. Such a tumor may cause limitation of ocular rotation but does so less frequently than does a meningioma, which generally affects the ocular muscles before it involves the optic nerve. He states a preference for the orbital over the intracranial route for the removal of such a tumor unless there is clinical or roentgenologic evidence of involvement of the intracanalicular or intracranial portion of the nerve. He does not think it necessary to do more than removal of the major portion of the tumor. He removed an astrocytoma from the right orbit of an 8-year-old girl by the Krönlein method. This girl and eight other members of her family in three generations were found to have neurofibromatosis. Marshall regards the presence of at least six café au lait spots of at least 15 mm. in diameter as diagnostic evidence of neurofibromatosis.

Streiff [202] states that it is only in the exceptional case that a tumor of the optic nerve can be removed leaving the globe in place. Roentgenograms of the optic canal should be made in every case of tumor of the optic nerve; transfrontal approach by the neurosurgeon is indicated if there is evidence of extension of the tumor into the canal. If evidence exists of infiltration of the cut end of the optic nerve after enucleation of the eye because of an intraocular tumor or after removal of an orbital tumor, a secondary transfrontal operation is necessary.

Manschot [225] states that a tumor of the optic nerve in Recklinghausen's disease is usually a glioma but may be a meningioma, an endothelioma, or simple fibromatosis. He reports manifestations of Reckinghausen's disease in several members of a family. A boy had a tumor of the chiasm and the left optic nerve and a subretinal tumor in the right eye. Both the boy and his twin sister were mentally deficient and had café au lait spots. The boy also had tiny fibromas in the skin and an intra-abdominal tumor. Another of his sisters had a proved glioma of the chiasm and the right optic nerve and café au lait spots. The mother had café au lait spots and cutaneous neurofibromas. Miller and Van Herick [226] report the occurrence of bilateral primary optic atrophy, more advanced in the right eye, in a patient with proved Recklinghausen's disease. Evidence of orbital involvement or of an intracranial mass lesion could not be found.

An unusual case of orbital tumor is reported by Mann and associates.[227] An astrocytoma of the optic nerve was removed from a 3-year-old child. Irradiation of the orbit resulted in a severe and extensive burn. A highly malignant meningioma developed in the irradiated region six years later. The frontal bone was involved, and intracranial extension proved fatal. Ryan [228] found in the blind left eye of a 6-year-old boy an elevated white mass, 3 disc diameters in size, that obscured the optic disc and protruded into the vitreous. Patches of atrophy of the choroid were visible around the mass. The eye was fixed in the orbit but was not proptosed. Roentgenograms of the optic canal showed nothing abnormal. The eye was enucleated, but it was impossible to remove all the involved portion of the optic nerve. The optic canal was found to be enlarged seven months later, and the residual part of the tumor was removed by the transfrontal route. Histologically the tumor was found to be a vascular psammomatous meningioma that had involved the choroid for a distance of 7 mm. around the optic nerve.

Histologic examination of an eye with progressive pigmentation of the optic disc observed by deVeer [229] revealed the presence of a juxtapapillary malignant melanoma of the choroid that had invaded the head of the optic nerve. Some of the pigment in the papilla was found to be in macrophages. This paper reviews reports of 10 cases previously described as primary malignant melanomas of the papilla; deVeer is not convinced that the existence of this entity had been definitely established. Scuderi [230] describes a lesion of the choroid and an associated papilledema that were proved histologically to be metastatic lesions in the choroid and optic papilla from carcinoma of the breast.

Seiwerth-Ferić [231] observed a reddish mass with a fine network of capillaries overlying the nasal, upper, and lower parts of the optic disc and extending into the nasal portion of the retina. It was about 2 to 3 disc diameters in size, was elevated 4 D., and was associated with edema of the retina and degeneration of the macula. The tentative diagnosis of angioendothelioma or angiosarcoma was made and, as progression occurred during a 10-month period of observation, enucleation was advised. This was refused and roentgen therapy was given. The patient was seen later by Franceschetti and Babel.[232] The mass was then elevated 7 D. and extended 2 disc diameters into the retina; a white patch with pigmented borders was present in the macula. The eye was enucleated. Histologic examination revealed cystoid degeneration of the entire retina with a large cyst on the nasal side of the optic disc. In the wall of this cyst was a minute capillary angioma originating from a branch of the central artery of the retina. The authors think that this case might be a monosymptomatic form of von Hippel-Lindau disease.

REFERENCES

1. Odell, J. E.: Current Concepts of Retrolental Fibroplasia, Am. Pract. & Digest Treat. **5**:416-421 (June) 1954.

2. Duke-Elder, S.: Retrolental Fibroplasia, Proc. Roy. Soc. Med. **47**:500 (June) 1954.

3. Jim, V. K. S., and Krause, A. C.: Electroencephalography in Retrolental Fibroplasia, Am. J. Ophth. **38**:337-341 (Sept.) 1954.

4. Ashton, N.: Pathological Basis of Retrolental Fibroplasia, Brit. J. Ophth. **38**:385-396 (July) 1954.

5. Reese, A. B., and Stepanik, J.: Cicatricial Stage of Retrolental Fibroplasia, Am. J. Ophth. **38**:308-316 (Sept.) 1954.

6. Owens, W. C.: Spontaneous Regression in Retrolental Fibroplasia, Tr. Am. Ophth. Soc. **51**: 555-579, 1953.

7. Locke, J. C.: Retrolental Fibroplasia: Definitive Role of Oxygen Administration in Its Etiology, A. M. A. Arch. Ophth. **51**:73-79 (Jan.) 1954.

8. Gordon, H. H.; Lubchenco, L., and Hix, I.: Observations on the Etiology of Retrolental Fibroplasia, Bull. Johns Hopkins Hosp. **94**:34-44 (Jan.) 1954.

9. Patz, A.: Clinical and Experimental Studies on Role of Oxygen in Retrolental Fibroplasia, Tr. Am. Acad. Ophth. **58**:45-50 (Jan.-Feb.) 1954.

10. Patz, A.: Oxygen Studies in Retrolental Fibroplasia: IV. Clinical and Experimental Observations, Am. J. Ophth. **38**:291-308 (Sept.) 1954.

11. Forrester, R. M.; Jefferson, E., and Naunton, W. J.: Oxygen and Retrolental Fibroplasia: A Seven-Year Survey, Lancet **2**:258-260 (Aug. 7) 1954.

12. Lanman, J. T.; Guy, L. P., and Dancis, J.: Retrolental Fibroplasia and Oxygen Therapy, J. A. M. A. **155**:223-226 (May 15) 1954.

13. Bedrossian, R. H.; Carmichael, P., and Ritter, J.: Retinopathy of Prematurity (Retrolental Fibroplasia) and Oxygen: I. Clinical Study; II. Further Observations on the Disease, Am. J. Ophth. **37**:78-86 (Jan.) 1954.

14. Fortier, E. G.: Therapeutic Possibilities of Carbon Dioxide in the Prevention of Retrolental Fibroplasia, Am. J. Ophth. **38**:342-348 (Sept.) 1954.

15. Fontaine, M.: Rétinopathie des prématurés, Arch. opht. **14**:140-153, 1954.

16. Hart, W. M.: Premature Infants: Management in a Community Hospital, South. M. J. **47**: 602-605 (June) 1954.

17. Denti, A., and Bernardi, M.: Retinopathy of the Premature Infant; abstracted, J. A. M. A. **155**: 1111-1112 (July 17) 1954.

18. Zacharias, L.; Reynolds, W. E.; Chisholm, J. F., Jr., and King, M. J.: Incidence and Severity of Retrolental Fibroplasia in Relation to Possible Causative Factors: I. Observations on the Occurrence of Retrolental Fibroplasia; II. Studies of the Relationship of Retrolental Fibroplasia to Degree of Prematurity, Oxygen Therapy, General Health, and Date of Birth of Premature Infants, Am. J. Ophth. **38**:317-336 (Sept.) 1954.

19. Blodi, F. C.: The Pathogenesis of Retrolental Fibroplasia, Am. Pract. & Digest Treat. **5**:413-414 (June) 1954.

20. Ingalls, T. H., and Purshottam, N.: Oxygenation and Retrolental Fibroplasia, New England J. Med. **250**:621-629 (April 15) 1954.

21. Apple, C.: Retrolental Fibroplasia, Am. J. Ophth. **37**:68-78 (Jan.) 1954.

22. Krause, A. C.: Blindness of Premature Infants; with Special Reference to Retrolental Fibroplasia, Illinois M. J. **104**:370-373 (Dec.) 1953.

23. Wolfe, O. R.: Surgical Treatment of Perilenticular Membranes in Children, J. Internat. Coll. Surgeons **21**:650-665 (May) 1954.

24. François, J.; Vanderstraeten, M., and Neetens, A.: Manifestations vasculaires de la rétine au cours de l'oxygenothérapie (Pathogénie de la fibroplasie rétrocristallienne), Ophthalmologica **128**:73-98 (Aug.) 1954.

25. Fletcher, M. C.: The Developing Fundus Oculi of the Premature Infant and Its Relationship to Retrolental Fibroplasia, J. Pediat. **43**:499-523 (Nov.) 1953.

26. Yoshioka, H.: Studies of the Eyes of Premature Infants; abstracted, Am. J. Ophth. **38**:760 (Nov.) 1954.

27. Ward, B. A.: Ocular Histology in Premature Infants with Reference to Retrolental Fibroplasia, Brit. J. Ophth. **38**:445-459 (Aug.) 1954.

28. Reese, A. B., and Blodi, F. C.: Hematopoiesis In and Around the Eye, Am. J. Ophth. **38**:214-221 (July, Pt. 2) 1954.

29. Gyllensten, L. J., and Hellström, B. E.: Experimental Approach to the Pathogenesis of Retrolental Fibroplasia: I. Changes of the Eye Induced by Exposure of Newborn Mice to Concentrated Oxygen, Acta pædiat., to be published.

30. Ashton, N.: Animal Experiments in Retrolental Fibroplasia, Tr. Am. Acad. Ophth. **58**:51-53 (Jan.-Feb.) 1954.

31. Ashton, N.; Ward, B., and Serpell, G.: Effect of Oxygen on Developing Retinal Vessels with Particular Reference to the Problem of Retrolental Fibroplasia, Brit. J. Ophth. **38**:397-432 (July) 1954.

32. Ashton, N., and Cook, C.: Direct Observation of the Effect of Oxygen on Developing Vessels: Preliminary Report, Brit. J. Ophth. **38**:433-440 (July) 1954.

33. Serpell, G.: Polysaccharide Granules in Association with Developing Retinal Vessels and with Retrolental Fibroplasia, Brit. J. Ophth. **38**:460-471 (Aug.) 1954.

34. Heinsius, E.: Durchblutungsstörungen der Netzhaut des Diabetikers, Klin. Monatsbl. Augenh. **125**:1-5, 1954.

35. Ehlers, H.: Ophthalmoscopical Findings in Proliferative Diabetic Retinopathy, Acta ophth. **31**: 289-297, 1953.

36. Hallum, A. V.: Ocular Manifestations of Diabetes, South. M. J. **47**:590-594 (June) 1954.

37. Howells, L. H.: Ocular Complications of Diabetes Mellitus, Brit. J. Ophth. **37**:716-724 (Dec.) 1953.

38. Miratynska-Rusinowa, E., and Lisiecka-Adamska, H.: Ocular Symptoms in Diabetics; abstracted, Am. J. Ophth. **38**:450 (Sept.) 1954.

39. Nonnenmacher, H.: Diabetes mellitus, Retinitis diabetica und Hypertonie während der Nachkriegszeit, Klin. Monatsbl. Augenh. **124**:579-583, 1954.

40. Portsmann, W., and Wiese, J.: Die retinopathie im Rahmen der diagetischen Angiopathie, Klin. Monatsbl. Augenh. **125**:336-354, 1954.

41. Fontana, G.: Contribution to the Problem of Diabetic Retinopathy and Insulin Treatment (Experimental Studies); abstracted, Am. J. Ophth. **38**: 427 (Sept.) 1954.

42. Dana, G. W.: The Type of Diabetes Mellitus Associated with Diabetic Retinitis, Diabetes **3**:210-212 (May-June) 1954.

43. Sauer, H., and Koch, H.: Retinopathia diabetica proliferans bei diabetischer Glomerulosklerose (Kimmelstiel-Wilson), Klin. Monatsbl. Augenh. **123**:395-404, 1953.

44. Lundbaek, K.: Diabetic Angiopathy: A Specific Vascular Disease, Lancet **1**:377-379 (Feb. 20) 1954.

45. Ditzel, J.: Morphologic and Hemodynamic Changes in the Smaller Blood Vessels in Diabetes Mellitus: I. Considerations Based on the Literature; abstracted, Am. J. Ophth. **38**:282 (Aug.) 1954.

46. Nastri, F., and d'Ermo, F.: Protein Content of the Blood of Diabetics with Retinopathy; abstracted, Am. J. Ophth. **38**:283 (Aug.) 1954.

47. Iannaccone, A., and Kornerup, T.: Plasma Lipids and Diabetic Retinopathy; abstracted, Am. J. Ophth. **38**:607 (Oct.) 1954.

48. Siliato, F.: Pathogenesis of Diabetic Retinopathy (Experimental Contribution and General Considerations); abstracted, Am. J. Ophth. **37**:305 (Feb.) 1954.

49. Becker, B.; Allen, R.; Winter, F. C.; Maengwyn-Davies, G., and Friedenwald, J. S.: The Role of the Adrenal Cortex and Vitamin B_{12} in Diabetic Retinopathy, Am. J. Ophth. **38**:53-58 (July, Pt. 2) 1954.

50. Becker, B.; Maengwyn-Davies, G. D.; Rosen, D.; Friedenwald, J. S., and Winter, F. C.: The Adrenal Cortex and B-Vitamins in Diabetic Retinopathy, Diabetes **3**:175-187 (May-June) 1954.

51. Goodman, J. I.: Vascular Lesions in Diabetes Mellitus: III. Pathogenesis, A. M. A. Arch. Ophth. **52**:108-120 (July) 1954.

52. Landaburu, P. B.; Davalos, R. C., and Jolly, C. H.: The Relationship Between the Severity and Care of Diabetes Mellitus and the Incidence of Diabetic Retinopathy; abstracted, Am. J. Ophth. **38**:607 (Oct.) 1954.

53. Beardwood, J. T., Jr., and Trueman, R. H.: Problem of Diabetic Retinopathy, J. Michigan M. Soc. **52**:1074-1079 (Oct.) 1953.

54. Scott, G. I.: Ocular Complications of Diabetes Mellitus, Brit. J. Ophth. **37**:705-715 (Dec.) 1953.

55. Bottoni, A.: Considerations on the Therapy of Diabetic Retinopathy; abstracted, Am. J. Ophth. **37**:624 (April) 1954.

56. Mehlhose, F.: Zur Problematik der Rutin-Wirkung bei der Retinopathia diabetica, Klin. Monatsbl. Augenh. **125**:5-13, 1954.

57. De Hoff, J. B., and Ozazewski, J.: Alpha Tocopherol to Treat Diabetic Retinopathy, Am. J. Ophth. **37**:581-582 (April) 1954.

58. Palmer, L., and Waldman, S.: Diabetic Retinopathy, A. M. A. Arch. Ophth. **51**:282-284 (Feb.) 1954.

59. Nordlöw, W.; Grönberg, A., and Svanteson, G.: Sexual hormonterapi vid retinopathia diabetica, Excerpta med. XII **8**:330 (Aug.) 1954.

60. Luft, R., and Olivecrona, H.: Experiences with Hypophysectomy in Man, J. Neurosurg. **10**: 301-316 (May) 1953.

61. Minsky, H.: Correlation of Ocular Changes in Essential Hypertension with Diastolic Blood Pressure, A. M. A. Arch. Ophth. **51**:863-874 (June) 1954.

62. Minsky, H.: Numerical Evaluation of Ocular Signs of Essential Hypertension; abstracted, Am. J. Ophth. **38**:608 (Oct.) 1954.

63. Olmsted, K. E. P.: Arteriosclerotic Diseases of the Retina, New York J. Med. **54**:784-787 (March 15) 1954.

64. Dehe, K. H.: Klinische Untersuchungen zum Kreuzungsphänomen an den Netzhautgefässen, von Graefes Arch. Ophth. **155**:167-186, 1954.

65. Wilson, F. M.: Ophthalmoscopic Evaluation of the Hypertensive Patient, Guildcraft **28**:17-24 (Jan.) 1954.

66. Taylor, R. D.; Corcoran, A. C., and Page, I. H.: Increased Cerebrospinal Fluid Pressure and Papilledema in Malignant Hypertension, A. M. A. Arch. Int. Med. **93**:818-824 (June) 1954.

67. Chesley, L. C.: Toxemia of Pregnancy, Am. J. M. Sc. **227**:683-699 (June) 1954.

68. Finnerty, F. A., Jr.: Does Vascular Damage Follow Toxemia of Pregnancy? An Internist's Appraisal of 303 Patients in a Toxemia Clinic, J. A. M. A. **154**:1075-1079 (March 27) 1954.

69. Meisner, G., and Unger, H.-H.: Augenveränderungen bei Neurofibromatosis und Phäochromozytom, Klin. Monatsbl. Augenh. **124**:466-472, 1954.

70. Bonnet, P.: Tortuosité congénitale des vaisseaux de la rétine et sténose congénitale de l'isthme de l'aorte. (Coarctation de l'aorte), Arch. opht. **14**:129-139, 1954.

71. Gifford, R. W., Jr.; Allen, E. V., and Birkhead, N. C.: Pentapyrrolidinium Bitartrate (M and B 2050A) in the Treatment of Hypertension: Preliminary Observations, Proc. Staff Meet., Mayo Clin. **29**:496-508 (Sept. 1) 1954.

72. Herbeuval, R.; Cuny, G.; Guidat, R., and Pinck, J.: Action du chlorhydrate de la 1-hydrazinophthalazine chez 60 hypertendus, Presse méd. **61**:1459-1460 (Nov. 11) 1953.

73. Herbeuval, R.; Cuny, G.; Mançiaux, M., and Guidat, R.: Study of an Alkaloid of "Rauwolfia Serpentina" in the Treatment of Arterial Hypertension; abstracted, J. A. M. A. **156**:202-203 (Sept. 11) 1954.

74. Livesay, W. R.; Moyer, J. H., and Miller, S. I.: Treatment of Hypertension with Rauwolfia Serpentina Alone and Combined with Other Drugs: Results in 84 Cases, J. A. M. A. **155**:1027-1035 (July 17) 1954.

75. Moyer, J. H.; Snyder, H. B.; Johnson, I.; Mills, L. C., and Miller, S. I.: Results with Oral Hexamethonium Alone and in Combination with 1-Hydrazinophthalazine (Apresoline) in the Therapy of Hypertension, Am. J. M. Sc. **225**:379-398 (April) 1953.

76. Smirk, F. H.: Results of Methonium Treatment of Hypertensive Patients, Based on 250 Cases Treated for Periods up to 3½ Years, Including 28 with Malignant Hypertension, Brit. M. J. **1**:717-723 (March 27) 1954.

77. Hughes, W.; Dennis, E.; McConn, R.; Ford, R., and Moyer, J. H.: Reserpine (Serpasil) in the Treatment of Hypertension, Am. J. M. Sc. **288**: 21-35 (July) 1954.

78. Herbst, W.: Beobachtungen über das verhalten hypertonischer Augenhintergrundveränderungen unter dem Einfluss von Hydergin, Klin. Monatsbl. Augenh. **124**:446-457, 1954.

79. Shapiro, A. P., and Grollman, A.: A Critical Evaluation of the Hypotensive Action of Hydrallazine, Hexamethonium, Tetraethylammonium and Dibenzyline Salts in Human and Experimental Hypertension, Circulation **8**:188-198 (Aug.) 1953.

80. Grob, D., and Langford, H. G.: Further Observations on the Effects of Autonomic Blocking Agents in Patients with Hypertension: I. General Systemic Effects of Hexamethonium, Pentamethonium and Hydrazinophthalazine, Circulation **8**:205-223 (Aug.) 1953.

81. Howard, J. E.; Berthrong, M.; Gould, D. M., and Yendt, E. R.: Hypertension Resulting from Unilateral Renal Vascular Disease and Its Relief by Nephrectomy, Bull. Johns Hopkins Hosp. **94**: 51-85, 1954.

82. Schaffer, A. J., and Markowitz, M.: Hypertension Treated by Nephrectomy: A Report of 4 Additional Cases and a Re-Evaluation of Prognosis and Criteria for Operation, Am. J. M. Sc. **227**: 417-425 (April) 1954.

83. Bowers, R. F.: Bilateral Adrenalectomy for Severe Hypertension, J. A. M. A. **154**:394-397 (Jan. 30) 1954.

84. Presto, E. C.: Total Amaurosis Following Parturition, Am. J. Ophth. **37**:586-587 (April) 1954.

85. Perese, D. M.; Kite, W. C.; Bedell, A. J., and Campbell, E.: Complications Following Cerebral Angiography, A. M. A. Arch. Neurol. & Psychiat. **71**:105-113 (Jan.) 1954.

86. Wittich, K.: "Embolie" einer Netzhautarterie infolge Retino-Choroiditis juxtapapillaris (E. Jensen), Klin. Monatsbl. Augenh. **123**:356-361, 1953.

87. Remler, O.: Hyderginanwendung bei Durchblutungsstörungen der Netzhaut, Klin. Monatsbl. Augenh. **124**:713-734, 1954.

88. Payne, I. W., and Reed, H.: Ocular Palsies Following Retrobulbar Injection of Acetyl Choline for Retinal Arterial Occlusion, Brit. J. Ophth. **38**: 46-48 (Jan.) 1954.

89. Guillette, J. L., and Mayer, W.: Thrombosis of the Central Retinal Artery: Report of a Successfully Treated Case, Am. J. Ophth. **37**:578-580 (April) 1954.

90. Ennema, M. C., and Zeeman, W. P. C.: Venous Occlusions in the Retina, Ophthalmologica **126**:329-354 (Dec.) 1954.

91. Wiedersheim, O.: Thrombose der Vena zentralis und Unfall, Klin. Monatsbl. Augenh. **122**: 484-489, 1953.

92. Lister, A., and Zwink, F. B.: The Course of Thrombosis of the Retinal Veins, Tr. Ophth. Soc. U. Kingdom **73**:55-68, 1953.

93. Dorello, U.: Treatment of Central Vein Thrombosis with Ethylic Ester of Acetic Acid (Tromexan); abstracted, Am. J. Ophth. **37**:160 (Jan.) 1954.

94. Siliato, F.: The Fibrolytic Enzyme in the Treatment of Thrombosis of the Central Retinal Vein; abstracted, Am. J. Ophth. **37**:305 (Feb.) 1954.

95. Hopen, J. M.: Use of Parenteral Trypsin in Acute Inflammatory and Thrombotic Ocular Disturbances, Am. J. Ophth. **38**:84-87 (July, Pt. 1) 1954.

96. Cliffton, E. E.: The Present Status of Therapeutic Use of Enzymes, Am. J. M. Sc. **228**:568-585 (Nov.) 1954.

97. Peck, M. E.: Preliminary Observations on the Effect of Trypsin Administered Intravenously, J. A. M. A. **154**:1260-1263 (April 10) 1954.

98. Taylor, A,; Overman, R. S., and Wright, I. S.: Studies with Crystalline Trypsin: Results and Hazards of Intravenous Administration and Its Postulated Role in Blood Coagulation, J. A. M. A. **155**:347-351 (May 22) 1954.

99. Fisher, M. M., and Wilensky, N. D.: Parenteral Trypsin in Peripheral Vascular and Thromboembolic Diseases, New York J. Med. **54**:659-662 (March 1) 1954.

100. Innerfield, I.: Trypsin Given Intramuscularly In Chronic, Recurrent Thrombophlebitis, J. A. M. A. **156**:1056-1058 (Nov. 13) 1954.

101. Hopen, J. M., and Campagna, F. N.: Use of Intramuscular Trypsin in Acute Inflammatory and Thrombotic Ocular Disturbances: A Preliminary Report, J. Philadelphia Gen. Hosp. **5**:20-25 (March) 1954.

102. Heptinstall, R. H.; Porter, K. A., and Barkley, H.: Giant-Cell (Temporal) Arteritis, J. Path. & Bact. **67**:507-519 (April) 1954.

103. Cordes, F. C.: Temporal Arteritis Syndrome with Ocular Involvement: A Report of 2 Cases, Am. J. Ophth. **38**:495-500 (Oct.) 1954.

104. Bässler, H.: Ein Fall von akuter, beidseitiger optikoretinaler Arteriitis granulomatosa bei Arteriitis temporalis, Klin. Monatsbl. Augenh. **125**:104-105, 1954.

105. Siegert, P.: Bemerkungen zu Kreibig: "Optikomalazie, die Folge eines Gefässverschlusses im retrobulbären Abschnitt des Sehnerven," Klin. Monatsbl. Augenh. **124**:337-338, 1954.

106. Schirmer, R.: Arteriitis temporalis mit Augenbeteiligung und Arterienresektion, Klin. Monatsbl. Augenh. **124**:58-63, 1954.

107. Bonnet, P.: L'artérite temporale et ses manifestations oculaires: Revue critique, Arch. opht. **14**: 24-47, 1954.

108. Krysta, F.: Arteriitis temporalis mit Augenbeteiligung, Klin. Monatsbl. Augenh. **122**:739-741, 1954.

109. Chapin, M. A., and Frost, R. A.: Temporal Arteritis: Treatment with Cortisone; 2 Case Reports, J. Maine M. A. **44**:304-308 (Nov.) 1953.

110. Meyerratken, E.: Über Augenveränderungen bei der Arteriitis temporalis und der Endangiitis obliterans, Klin. Monatsbl. Augenh. **123**: 433-439, 1953.

111. Kimura, S. J.; Hogan, M. J., and Thygeson, P.: Uveitis in Children, A. M. A. Arch. Ophth. **51**:80-88 (Jan.) 1954.

112. Long, K. M.: Congenital Toxoplasmosis, Brit. J. Ophth. **38**:123-125 (Feb.) 1954.

113. Masters, S.: Toxoplasmosis: A Report of the Literature and Clinical Studies Based on 5 Cases, Am. J. Ophth. **38**:194-200 (Aug.) 1954.

114. Hill, J.: Congenital Toxoplasmosis, Brit. J. Ophth. **37**:689-693 (Nov.) 1953.

115. Lavat, J.: Toxoplasmoses oculaires, Arch. opht. **13**:252-271, 1953.

116. Glees, M.: Beiderseitiger Mikrophthalmus bei nachgewiesener konnataler Toxoplasmoses: Klinische und histologische Beobachtungen, Ophthalmologica **126**:361-368 (Dec.) 1953.

117. Jacobs, L.; Cook, M. K., and Wilder, H. C.: Serologic Data on Adults with Histologically Diagnosed Toxoplasmic Chorioretinitis, Tr. Am. Acad. Ophth. **58**:193-198 (March-April) 1954.

118. Woods, A. C.; Jacobs, L.; Wood, R. M., and Cook, M. K.: Study of the Role of Toxoplasmosis in Adult Chorioretinitis, Am. J. Ophth. **37**:163-177 (Feb.) 1954.

119. Woods, A. C.; Jacobs, L.; Wood, R. M., and Cook, M. K.: Study of the Role of Toxoplasmosis in Adult Chorioretinitis, Tr. Am. Acad. Ophth. **58**: 172-188 (March-April) 1954.

120. Hudson, J. R.: Toxoplasmic Choroido-Retinitis in the Adult, Brit. J. Ophth. **38**:179-181 (March) 1954.

121. Hudson, J. R.: Clinical Aspects of Toxoplasmosis, in Discussion: Toxoplasmosis, Proc. Roy. Soc. Med. **47**:484-488 (June) 1954.

122. Fair, J. R.: Uveitis: A Military Problem, A. M. A. Arch. Ophth. **51**:364-368 (March) 1954.

123. Smith, C. H.: Histological Appearances, in Discussion: Toxoplasmosis, Proc. Roy. Soc. Med. **47**:481-484 (June) 1954.

124. Carreras Duran, B.: Periphlebitis of the Retina and Toxoplasmosis; abstracted, Am. J. Ophth. **38**:759 (Nov.) 1954.

125. Jacobs, L.; Fair, J. R., and Bickerton, J. H.: Adult Ocular Toxoplasmosis: A Preliminary Report of a Parasitologically Proved Case, A. M. A. Arch. Ophth. **51**:287 (March) 1954.

126. Jacobs, L.; Fair, J. R., and Bickerton, J. H.: Adult Ocular Toxoplasmosis: Report of a Parasitologically Proved Case, A. M. A. Arch. Ophth. **52**:63-71 (July) 1954.

127. Eyles, D. E.: Present Status of the Chemotherapy of Toxoplasmosis, Am. J. Trop. Med. **2**: 429-444 (May) 1953.

128. Beverley, J. K. A.; Beattie, C. P., and Fry, B. A.: Experimental Toxoplasmosis of the Uveal Tract, Brit. J. Ophth. **38**:489-496 (Aug.) 1954.

129. Saggese, D. A.: The Fundus in Tuberculous Meningitis in Children, Am. J. Ophth. **37**:215-219 (Feb.) 1954.

130. Obal, A.: Augenbefunde bei Meningitis tbc. nach Streptomycin- und Isonikotinsäurehydrazidbehandlung, Klin. Monatsbl. Augenh. **122**:584-599, 1953.

131. Cremer, M., and Cremer, M., Jr.: Untersuchungen über die Verwertbarkeit der Hämagglutinationsreaktion nach Middlebrook und Dubos zur ätiologischen Klärung tuberkulöser Augenerkrankungen, von Graefes Arch. Ophth. **155**:485-491 (Aug. 19) 1954.

132. Juszkowa, K.: Treatment of Tuberculous Diseases of the Eye with Streptomycin; abstracted, Am. J. Ophth. **38**:125 (July, Pt. 1) 1954.

133. Schlaegel, T. F., Jr., and Hungerford, L. N., Jr.: Isoniazid in Tuberculous Uveitis, A. M. A. Arch. Ophth. **51**:481-498 (April) 1954.

134. Woods, A. C.; Becker, B., and Wood, R. M.: Studies in Experimental Ocular Tuberculosis: XVII. Effect of Isoniazid in the Normal, Nonimmune Rabbit, A. M. A. Arch. Ophth. **51**:242-255 (Feb.) 1954.

135. Woods, A. C.: Pathogenesis and Treatment of Ocular Tuberculosis, A. M. A. Arch. Ophth. **52**: 174-196 (Aug.) 1954.

136. Pajtáš, J.: Zur Heilung der Periphlebitis tuberculosa mittels Elektrokoagulation, mit Streptomycin und PAS kombiniert, Ophthalmologica **126**:116-122 (Aug.) 1953.

137. Franceschetti, A., and Forni, S.: Le traitement chirurgical des hémorragies récidivantes rétino-vitréennes des jeunes sujets (maladie d'Eales), Ophthalmologica **127**:339-341 (April-May) 1954.

138. Foggitt, K. D.: Ocular Disease Due to Brucellosis, Brit. J. Ophth. **38**:273-278 (May) 1954.

139. Tanner, O. R.: Ocular Manifestations of Infectious Mononucleosis, A. M. A. Arch. Ophth. **51**: 229-241 (Feb.) 1954.

140. Brihaye-van Geertruyden, M.; Danis, P., and Toussaint, C.: Fundus Lesions with Disseminated Lupus Erythematosus, A. M. A. Arch. Ophth. **51**:799-810 (June) 1954.

141. Tumulty, P. A.: Clinical Course of Systemic Lupus Erythematosus, J. A. M. A. **156**:947-953 (Nov. 6) 1954.

142. Kiel, E.: Über die Erkrankung des Auges durch Fliegenlarven, Klin. Monatsbl. Augenh. **124**: 194-200, 1954.

143. Galewska, Z.: A Case of Ophthalmomyiasis Interna in a 5-Year-Old Boy, Excerpta med. XII. **8**:309 (Aug.) 1954.

144. Hartmann, K.: Bemerkungen zu der Arbeit Kiel "Über die Erkrankung des Auges durch Fliegenlarven," Klin. Monatsbl. Augenh. **125**:227-230, 1954.

145. Sansone, G., and Mariotti, L.: Ocular Manifestations of Acute Leucemia in Childhood with Special Consideration of Leucemic Retinopathy; abstracted, Am. J. Ophth. **37**:303 (Feb.) 1954.

146. Henry, M. D., and Chapman, A. Z.: Vitreous Hemorrhage and Retinopathy Associated with Sickle-Cell Disease, Am. J. Ophth. **38**:204-209 (Aug.) 1954.

147. Rudd, C.; Evans, P. J., and Peeney, A. L. P.: Ocular Complications in Thalassaemia Minor, Brit. J. Ophth. **37**:353-358 (June) 1953.

148. Cagianut, B., and Hoffmann-Egg, L.: Über Augenhintergrundsveränderungen bei Makroglobulinämien, von Graefes Arch. Ophth. **153**:391-406 (May 20) 1953.

149. Berneaud-Kötz, G., and Jahnke, K.: Über einen Fall von ungewöhnlicher Dys- und Paraproteinämie mit auffallenden Augenhintergrundveränderungen (Fundus paraproteinaemicus), Klin. Monatsbl. Augenh. **125**:160-171, 1954.

150. Farnarier, G., and Sobrepère, G.: L'élastorrexie systématisée (Stries angioïdes, pseudoxanthome élastique, dégénérescence élastique artérielle), Arch. opht. **13**:472-477, 1953.

151. François, J., and Verriest, G.: Les fonctions visuelles dans l'élastose rétinienne (rétinopathie à stries angioïdes), Ann. ocul. **187**:113-144 (Feb.) 1954.

152. Cowper, A. R.: Angioid Streaks: Tears in Bruch's Membrane or Pigmented Choroidal Vessels (?), A. M. A. Arch. Ophth. **51**:762-782 (June) 1954.

153. Bossu, A., and Lambrechts: Manifestations oculaires du syndrome d'Ehlers-Danlos, Ann. ocul. **187**:227-236 (March) 1954.

154. Pietruschka, G.: Zur Frage der Augenveränderungen bei der Ostitis deformans Paget in Beziehung zur Arteriosklerose, Klin. Monatsbl. Augenh. **125**:171-183, 1954.

155. Kehler, A.: Optic Atrophy and Retinal Changes Following Thoracic Trauma: Survey of the Relationship Between Traumatic Retinal Angiopathy (Purtscher), Traumatic Asphyxia and Fat Embolism and Report of a Case, Acta ophth. **31**:437-456, 1953.

156. Thomas, C.; Cordier, J.; Algan, B., and Fiel, J.: Les accidents visuels au cours des interventions pleurales, Arch. opht. **14**:5-23, 1954.

157. Velzeboer, C. M. J.: Ocular Manifestations in Löffler's Syndrome, Brit. J. Ophth. **37**:731-740 (Dec.) 1953.

158. Haarr, M.: Periphlebitis Retinae in Association with Multiple Sclerosis: Contribution to the Discussion on the Pathogenesis of Multiple Sclerosis, Acta psychiat. et neurol. **28**:175-190, 1953.

159. Vanni, V., and Frugoni, P.: Rare Ocular Manifestations of Raynaud's Disease; abstracted, Am. J. Ophth. **38**:284-285 (Aug.) 1954.

160. Caccamise, W. C., and Okuda, K.: Takayasu's or Pulseless Disease: An Unusual Syndrome with Ocular Manifestations, Am. J. Ophth. **37**:784-786 (May) 1954.

161. Jervell, A.: Pulseless Disease, Am. Heart J. **47**:780-784 (May) 1954.

162. Ashton, N.: Pulseless Disease and Oxygen Studies, Am. J. Ophth. **38**:418 (Sept.) 1954.

163. Givner, I.: Visual Loss Following Cardiac Arrest, A. M. A. Arch. Ophth. **51**:878-879 (June) 1954.

164. Duane, T. D.: Observations on the Fundus Oculi During Black-Out, A. M. A. Arch. Ophth. **51**:343-355 (March) 1954.

165. Huber, A.: Relationship Between the Retinal and the Cerebral Vessels, Tr. Ophth. Soc. U. Kingdom **73**:517-529, 1953.

166. Silver, M. L.: Hereditary Vascular Tumors of the Nervous System, J. A. M. A. **156**:1053-1056 (Nov. 13) 1954.

167. Kent, L. R.: A Case of Retinal Hemangiomatosis Treated with Diathermy, A. M. A. Arch. Ophth. **51**:409-410 (March) 1954.

168. Straatsma, B. A.: Angiomatosis Retinae, New England J. Med. **250**:314-317 (Feb. 25) 1954.

169. Sapuppo, C.: Syndrome of Morgagni with an Angioma of the Retina; abstracted, Am. J. Ophth. **38**:608-609 (Oct.) 1954.

170. Piper, H. F.: Über cavernöse Angiome in der Netzhaut, Ophthalmologica **128**:99-107 (Aug.) 1954.

171. Riffenburgh, R. S.: Arteriovenous Aneurysm of the Retina, Am. J. Ophth. **37**:908-910 (June) 1954.

172. Glees, M.: Arteriovenöses Aneurysma des Augenhintergrundes und der gleichseitigen Grosshirnhemisphäre (Klinische Beobachtungen und dynamometrische Bestimmungen), Klin. Monatsbl. Augenh. **124**:457-460, 1954.

173. Manschot, W. A.: Subarachnoid Hemorrhage: Intraocular Symptoms and Their Pathogenesis, Am. J. Ophth. **38**:501-505 (Oct.) 1954.

174. Stallard, H. B.: Annular Peripheral Retinal Detachment, Brit. J. Ophth. **38**:115-118 (Feb.) 1954.

175. Agarwal, L. P.: Double Balloon Formation in Detachment of Retina, Acta ophth. **32**:123-129, 1954.

176. Rais; Ben Slimane, and Mrad: Un cas de latéro-version de la rétine, Arch. opht. **13**:773-775, 1953.

177. Favre, M.: Trous parapapillaires comme cause du décollement de la rétine, Ophthalmologica **127**:351-354 (April-May) 1954.

178. Simonelli, M., and Faldi, S.: Better View of Retinal Tears After Intravenous Injection of Fluorescein and Geigy Blue; abstracted, Am. J. Ophth. **37**:628 (April) 1954.

179. Mawas, J.: L'épithélium pigmentaire de la rétine, Ann. ocul. **186**:488-506 (June) 1953.

180. Arruga, H.: Sur la pathogénie et le traitement post-opératoire du décollement rétinien, Ann. ocul. **186**:507-510 (June) 1953.

181. Massin, M.: Les décollements traumatiques de la rétine, Arch. opht. **14**:154-171, 1954.

182. Vannas, S., and Voipio, H.: Bilateral Juvenile Retinal Detachment with Symmetrical Oral Dialyses, Acta ophth. **32**:63-68, 1954.

183. Westsmith, R. A., and Abernethy, R. E.: Detachment of Retina with Use of Diisopropyl Fluorophosphate (Flurcpryl) in Treatment of Glaucoma, A. M. A. Arch. Ophth. **52**:779-780 (Nov.) 1954.

184. Paycha, F. C.: Étude du rôle prédisposant de la carence en vitamine A dans le décollement de la rétine, Arch. opht. **13**:*272-276*, 1953.

185. Stagni, S.: Relation Between the Insertion of the Extrinsic Muscles of the Eye and the Site of Retinal Tears; abstracted, Am. J. Ophth. **38**: *275* (Aug.) 1954.

186. Alajmo, A., and Auricchio, G.: Experimental Detachment of the Retina; abstracted, Am. J. Ophth. **37**:158 (Jan.) 1954.

187. Dellaporta, A.: Endodiathermy: A Method for Sealing Macular Holes by Transbulbar Coagulation, Am. J. Ophth. **37**:649-656 (May) 1954.

188. Bonavolontà, G.: Clinical Considerations on Some Aspects of Diathermic Retinochoroiditis in Detachment of the Retina; abstracted, Am. J. Ophth. **38**:*271* (Aug.) 1954.

189. Bangerter, A.: Zur Therapie der Netzhautablösung, Ophthalmologica **127**:346-350 (April-May) 1954.

190. Koenig, I. J.: The Place for Scleral Shortening Procedure in Retinal Detachment, Eye Digest **1**:25-31 (Aug.) 1954.

191. Böhringer, H. R.: Zur lamellären Skleraresektion bei Netzhautablösung, Ophthalmologica **127**:342-345 (April-May) 1954.

192. Dellaporta, A. N.: Comparison of Scleral Resection and Scleral Folding in Experimental Shortening of the Eye, A. M. A. Arch. Ophth. **51**: 525-534 (April) 1954.

193. Shapland, C. D.: Changes in the Refraction of the Eye Following the Operation of Lamellar Scleral Resection, Tr. Ophth. Soc. U. Kingdom **73**: *205-237*, 1953.

194. Lindner, K.: Die operative Behandlung hochgradiger Myopie gelegentlich einer Netzhautablhebung, Wien. klin. Wchnschr. **66**:8-10 (Jan. 8) 1954.

195. Frey, R. G.: Die Entwicklung der chirurgischen Behandlung der Netzhautablhebung an der II. Univ.-Augenklinik in Wien, Klin. Monatsbl. Augenh. **125**:329-336, 1954.

196. Kronfeld, P. C., and Pischel, D. K.: Scleral Resection Operation for Retinal Detachment: An Evaluation of the Results, A. M. A. Arch. Ophth. **51**:*356-363* (March) 1954.

197. Infante, F.: Scleral Resection as an Aid in the Treatment of Retinal Detachment; abstracted, Am. J. Ophth. **37**:300 (Feb.) 1954.

198. Basterra, J.: Scleral Resection Combined with Diathermy in the Treatment of Cases of Retinal Detachment with a Poor Prognosis; abstracted, Am. J. Ophth. **37**:624 (April) 1954.

199. Rumpf, J.: Le destin de l'oeil opéré avec succès d'un décollement de la rétine, Ophthalmologica **127**:100-104 (Feb.) 1954.

200. Scher, D.: Systemic Complications of Retinal Detachment Surgery, Am. J. Ophth. **37**:582-585 (April) 1954.

201. Rintelen, F.: Zur Prognose des Retinoblastoms, Ophthalmologica **127**:253-254 (April-May) 1954.

202. Streiff, E. B.: Le traitement chirurgical des tumeurs malignes de l'oeil et de ses annexes, Ophthalmologica **127**:*262-276* (April-May) 1954.

203. Stallard, H. B.: Pathological Study of Retinoblastoma Treated by Radon Seeds and Radium Disks, A. M. A. Arch. Ophth. **51**:573-588 (May) 1954.

204. Dollfus, M.-A.: Le traitement des tumeurs du globe oculaire et de l'orbite par les irradiations, Ophthalmologica **127**:*226-241* (April-May) 1954.

205. Dunphy, E. B.; Dreisler, K. K.; Cadigan, J. B., and Sweet, W.: Uptake of Radioactive Phosphorus by Intraocular Neoplasms, Am. J. Ophth. **37**:45-54 (Jan.) 1954.

206. Thomas, C. I.; Krohmer, J. S., and Storaasli, J. P.: Geiger Counter Probe for Diagnosis and Localization of Posterior Intraocular Tumors, A. M. A. Arch. Ophth. **52**:413 (Sept.) 1954.

207. Bettman, J. W., and Fellows, V.: Radioactive Phosphorus as a Diagnostic Aid in Ophthalmology, A. M. A. Arch. Ophth. **51**:171-179 (Feb.) 1954.

208. Thomas, C. I.; Krohmer, J. S.; Storaasli, J. P., and Friedell, H. L.: Detection of Intraocular Tumors by the Use of Radioactive Phosphorus, Am. J. Ophth. **38**:93-99 (July, Pt. 2) 1954.

209. Eisenberg, I. J.; Leopold, I. H., and Sklaroff, D.: Use of Radioactive Phosphorus in Detection of Intraocular Neoplasms, A. M. A. Arch. Ophth. **51**:633-641 (May) 1954.

210. Eisenberg, I. J.; Terner, I. S., and Leopold, I. H.: Use of P^{32} as an Aid in Diagnosis of Intraocular Neoplasms: Further Observations, A. M. A. Arch. Ophth. **52**:741-750 (Nov.) 1954.

211. Town, A. E.: Differential Diagnosis Between Solid and Serous Detachment of the Retina, Pennsylvania M. J. **56**:1046-1048 (Dec.) 1953.

212. Stephenson, R. W.: Hereditary Retinal Abiotrophies, Tr. Ophth. Soc. U. Kingdom **73**: 611-615, 1953.

213. Strazzi, A.: Retinitis Pigmentosa and Endocrine Disturbances; abstracted, Am. J. Ophth. **38**: 275 (Aug.) 1954.

214. Jager, G. M.: A Hereditary Retinal Disease, Tr. Ophth. Soc. U. Kingdom **73**:617-619, 1953.

215. Rosehr, K.: Über den weiteren Verlauf der von Stargardt und Behr beschriebenen familiären Degeneration der Makula, Klin. Monatsbl. Augenh. **124**:171-179, 1954.

216. Oksala, A.: Juvenile Macular Dystrophy, Acta ophth. **31**:385-394, 1953.

217. Klien, B. A.: Late Infantile Amaurotic Idiocy: A Clinico-Histopathologic Study, Am. J. Ophth. **38**:470-475 (Oct.) 1954.

218. François, J., and Neetens, A.: Vascularization of the Optic Pathway: I. Lamina Cribrosa and Optic Nerve, Brit. J. Ophth. **38**:472-488 (Aug.) 1954.

219. Smith, H. E.: Aplasia of the Optic Nerve: Report of Three Cases, Am. J. Ophth. **37**:498-504 (April) 1954.

220. Zweng, H. C.: Congenital Neuroepithelial Cyst of the Optic Nerve, Kresge Eye Inst. Bull. **5**:46-49 (May) 1954.

221. Jaeger, W.: Dominant vererbte Opticusatrophie. (Unter besonderer Berücksichtigung der dabei vorhandenen Farbensinnstörung.), von Graefes Arch. Ophth. **155**:457-484 (Aug. 19) 1954.

222. Huerkamp, B.: Ophthalmoskopische Befunde und Netzhautsymptome bei Leberscher Optikusatrophie, Klin. Monatsbl. Augenh. **124**:164-170, 1954.

223. Teuns, J.: Optic Neuritis Caused by Virus of Epidemic Parotitis; abstracted, J. A. M. A. **156**: 1289 (Nov. 27) 1954.

224. Marshall, D.: Glioma of the Optic Nerve as a Manifestation of von Recklinghausen's Disease, Am. J. Ophth. **37**:15-33 (Jan.) 1954.

225. Manschot, W. A.: Primary Tumours of the Optic Nerve in von Recklinghausen's Disease, Brit. J. Ophth. **38**:285-289 (May) 1954.

226. Miller, W. A., and Van Herick, W.: Primary Optic Atrophy in von Recklinghausen's Disease: Report of a Case, Am. J. Ophth. **37**:36-41 (Jan.) 1954.

227. Mann, I.; Yates, P. C., and Ainslie, J. P.: Unusual Case of Double Primary Orbital Tumour, Brit. J. Ophth. **37**:758-762 (Dec.) 1953.

228. Ryan, Hugh: Intra-Orbital Meningioma of the Optic Nerve, Brit. J. Ophth. **37**:506-507 (Aug.) 1953.

229. deVeer, J. A.: Juxtapapillary Malignant Melanoma of the Choroid and So-Called Malignant Melanoma of the Optic Disk: A Pathologic Study, A. M. A. Arch. Ophth. **51**:147-160 (Feb.) 1954.

230. Scuderi, G.: Metastatic Carcinoma of the Optic Papilla and the Choroid (Clinical and Histological Study); abstracted, Am. J. Ophth. **38**:607 (Oct.) 1954.

231. Seiwerth-Ferić, F.: Tumor papillae nervi optici, Ophthalmologica **127**:105-110 (Feb.) 1954.

232. Franceschetti, A., and Babel, J.: Microangiome avec dégénérescence kystique de la rétine (Forme monosymptomatique d'une maladie de von Hippel-Lindau?), Ophthalmologica **128**:23-29 (July) 1954.

Special Report

INTERNATIONAL COUNCIL OF OPHTHALMOLOGY AND INTERNATIONAL FEDERATION OF OPHTHALMOLOGICAL SOCIETIES

Résumé of Minutes of Meetings Held at the Seventeenth International Congress of Ophthalmology, at Montreal, Canada, Sept. 9-11, 1954

INTERNATIONAL COUNCIL OF OPHTHALMOLOGY

Apart from current business, the following is a summary of the main decisions taken.

I. *International Standardizations.*—The main business of the meeting concerned the international standardization of visual requirements for transport workers. The reports of the committees dealing with the standardization of optotypes, the color sense, and the limits of spectacle correction recommended for transport workers were considered and referred to the Federation for confirmation. A scheme for the codification of the colors of labels of ophthalmic drugs was also agreed. These recommendations will be noted in the Minutes of the Federation.

II. *Ophthalmological Education.*—The Council considered the report presented by Alvaro on behalf of the committee which had been studying the question of ophthalmological education. The report was thought to be of such importance that it was decided to submit it to the principal ophthalmic journals in the world for publication.

III. *International Dictionary of Ophthalmic Terms.*—The committee concerned reported on the progress of the "International Dictionary of Ophthalmic Terms," and it is hoped that this dictionary, which contains such terms in six languages (German, English, Spanish, French, Italian, and Latin), will appear in the near future.

IV. *Index Ophthalmologicus.*—The publication of the new "Index Ophthalmologicus" was considered, and the Council thanked Dr. A. C. Copper for his excellent work in its preparation. This new Index contains a résumé of the Council's activities, and a list of the names and addresses of ophthalmologists in most countries of the world, as well as particulars of the ophthalmic hospitals, societies for the blind, ophthalmological societies, and ophthalmic journals. The Index can be obtained from Dr. A. C. Copper, 97 Nieuwstad, Zutphen, Netherlands, for the sum of $2.75 (£1 sterling), or its equivalent.

V. *Affiliation of New Societies.*—The Council approved the requests for affiliation of certain ophthalmological societies (Australia, Colombia, India, and Venezuela).

VI. Recommendations were made to the Federation with regard to the 18th International Congress, and the next meeting of the Council was fixed to take place in Paris, on May 7, 1955.

INTERNATIONAL FEDERATION OF OPHTHALMOLOGICAL SOCIETIES

The main business was as follows:

I. *New Statutes.*—The new Statutes regulating the activities of the International Council, the International Federation, and International Congresses were

studied and, with minor amendments, were provisionally accepted until their final consideration, in 1958. According to these Statutes, every endeavor is to be made to keep national delegates (and through them, their societies) acquainted with the work of the International Council.

II. *Subscription.*—The subscription for member societies to the Federation was retained without modification, that is, at the rate of ½ Swiss franc per member.

III. *International Standardizations.*—The recommendations of the Council on international standardization in examining candidates for public transport were considered, as well as the Council's recommendations on the labeling of ophthalmic drugs. The essential recommendations are shown in an appendix.

IV. *XVIII International Congress of Ophthalmology.*—It was decided that the next Congress should be held in September, 1958, in Brussels, with Prof. Léon Coppez as President; this country was chosen as a compliment to the Belgians in view of the fact that this would be a centenary meeting, the first Congress having been held in 1857, in Belgium.

V. *New International Council.*—The new International Council was elected as follows:

President of the Council (and of the Federation).....Duke-Elder (Great Britain)
Vice-president of the Council (and of the Federation)...Berens (United States)
Secretary of the Council (and of the Federation).....Hartmann (France)
Treasurer of the Council (and of the Federation).....Amsler (Switzerland)
President of the International Association for the Prevention of Blindness.....Franceschetti (Switzerland)
President of the International Organization Against Trachoma.....Bietti (Italy)
President of the Pan-American Association of Ophthalmology.....To be filled in 1956
Retiring President of the Congress.....Samuels (United States)
President of the next Congress.....Coppez (Belgium)

Ordinary members:

Alvaro (Brazil); Arruga (Spain); Charamis (Greece); Palomino Dena (Mexico); Duggan (India); Lyle (Great Britain); Marshall (Canada); Paufique (France); Thiel (Germany); Weve (Netherlands).

APPENDIX

1. *Tables for Transcription of the Acuity of Vision from the Decimal System.*—For some decimals the distance at the examination has to be altered from 6 to 5 meters, or from 20 to 15 ft.

	Snellen's 6-Meter Tables		
1.0	6/6	0.5	6/12
0.8	5/6	0.4	5/12
0.7	6/9	0.3	6/18
0.6	5/9	0.1	6/60
	20-Foot Tables		
1.0	20/20	0.5	20/40
0.8	20/25	0.4	20/50
0.7	20/30	0.3	20/70
0.6	15/25	0.1	20/200
	Resolution Angle Tables		
1.0	1.0	0.5	2.0
0.9	1.1	0.4	2.5
0.8	1.3	0.3	3.3
0.7	1.4	0.2	5.0
0.6	1.6	0.1	10.0

2. *Color Sense.*—The color sense will be tested by isochromatic tables. At present the Ishihara tables are recommended. Others which may be found to be equally good or better in the future will also be recommended.

3. *Tonometry.*—The Schiøtz tonometer is recommended as conforming to the specifications of the Committee on Standardization of Tonometry of the American Academy of Ophthalmology and Otolaryngology.

4. *Spectacles for Public Transport.*—Recommendations for the spectacles allowable for candidates for public transport are as follows:

Concave spherical lenses	—7 D. maximum
Convex spherical lenses	+4 D. maximum
Cylindrical lenses	±4 D. maximum

Unshatterable lenses advisable

Periscopic lenses advisable

Tinted lenses advisable only in bright daylight

Stability of the mounting of spectacles important

Provision of a second pair of spectacles as replacements advisable

Contact lenses acceptable if previously tolerated for three months

5. *Labeling of Ophthalmic Drugs.*—It is recommended that the labels of ophthalmic medications should be different colors, depending on their nature, as follows:

(*a*) Red—drugs that in certain circumstances can be dangerous, e. g., mydriatics

(*b*) Orange—drugs to be used with caution, e. g., miotics, cortisone, tolazoline (Priscol), epinephrine (Adrenalin), antibiotics, isofluorophate (Fluoropropyl), etc.

(*c*) Green—drugs without danger, e. g., silver preparations, zinc sulfate, mild antiseptics, antazoline (Antistin), naphazoline (Privine), etc.

(*d*) Red with green bands—anesthetics

Correspondence

BALINT'S SYNDROME AND OCULAR MOTOR APRAXIA

To the Editor:—A recent article by H. Hécaen and J. de Ajuriaguerra (Balint's Syndrome [Psychic Paralysis of Visual Fixation] and Its Minor Forms, *Brain* **77**:373-400, 1954) has drawn our attention to a description by Balint in 1909 in the German literature and to a subsequent description by the foregoing authors in the French literature of an entity which may well be the same as that we have recently described under the heading of "Ocular Motor Apraxia" (A. M. A. Arch. Ophth. **50**: 434-442, 1953). By whatever name one wishes to call them, these cases should probably be considered together. The patient described by Balint showed (1) inability to look toward a point in the peripheral field voluntarily but full ocular movements when higher psychological functions were not involved, (2) full "proprioceptive control" of ocular movements, and (3) specific inattention for visual stimuli, noted particularly for objects in the peripheral field. The cause of the syndrome was bilateral (although asymmetric) softening in the parietal regions and corpus callosum. Unfortunately, Balint's description of the ocular motor deficit was not sufficient for us to accept it unreservedly in the entity of ocular motor apraxia, but the other aspects of the case make it seem a likely instance of this entity.

Hécaen and de Ajuriaguerra refer to a case of Balint's syndrome which they previously described in conjunction with several other authors (*Rev. neurol.* **83**:81, 1950). The most striking feature was the "locking of fixation," but the case showed all three of the characteristics of Balint's syndrome, and also apraxia in the non-visual spheres. In the present article the authors present three cases which they interpret as minor forms of Balint's syndrome. All had some form of apraxia and may well have had apraxia of the ocular motor variety, although complications (amaurosis, alexia, and agnosia) made the cases less clear-cut examples of the entity. They all had bilateral cerebral lesions with predominant involvement of the parieto-occipital region.

In our report we were able to find three cases in the literature which we felt were unequivocal instances of ocular motor apraxia. The first of these was reported by Wilson in 1908, that is, one year prior to Balint's article.

These cases, and the two which we described, were characterized by loss of volitional control of the eyes but preservation of full random movements. An entity occurring in children has also been described by one of us as a congenital variant of this entity (*Tr. Am. Acad. Ophth.* **56**:853-862, 1952).

It is not our intent to belabor the terminology as to whether this entity should be called Balint's syndrome or ocular motor apraxia, but, rather, we wish to point out that the two are probably one and the same syndrome. Thus the total number of reported cases allegedly bearing on this entity is 10 of the acquired variety and 4 of the congenital variety.

David G. Cogan, M.D.
Raymond D. Adams, M.D.
243 Charles St.
Boston 14.

News and Comment

EDITED BY DR. W. L. BENEDICT

ANNUAL MEETING OF AMERICAN MEDICAL ASSOCIATION

Atlantic City, N. J., June 6-10, 1955

Combined Meeting of Section on Ophthalmology with Association for Research in Ophthalmology

SECTION ON OPHTHALMOLOGY

Tuesday Morning—June 7

Chairman's Address
ERLING W. HANSEN, Minneapolis

Address of Invited Foreign Guest
J. W. TUDOR THOMAS, Cardiff, Wales

Fuchs's Syndrome of Heterochromic Cyclitis: Analysis of Thirty Cases
SAMUEL J. KIMURA, MICHAEL J. HOGAN, and PHILLIPS THYGESON, San Francisco
Discussion to be opened by PARKER HEATH, Sullivan, Maine

Circulatory Disturbances of the Retina with Particular Reference to Therapeutic Procedure
BANKS ANDERSON, Durham, N. C.
Discussion to be opened by ARTHUR J. BEDELL, Albany, N. Y.

Some Instructive Manifestations of Chiasmal Disease: One Case of Pituitary Adenoma, One of Optochiasmic Neuritis (Arachnoiditis), and One of Chiasmal Glioma
JOHN P. WENDLAND, Minneapolis
Discussion to be opened by JOHN WOODWORTH HENDERSON, Ann Arbor, Mich.

Therapeutic Studies in Experimental Chemical Injury of the Cornea
GUSTAV C. BAHN and JAMES H. ALLEN, New Orleans
Discussion to be opened by HEDWIG S. KUHN, Hammond, Ind.

Etiology of Retinochoroiditis and Uveitis
J. V. CASSADY, CARL S. CULBERTSON, and JAMES A. BAHLER, South Bend, Ind.
Discussion to be opened by HARRY FELDMAN, Syracuse, N. Y.

Glaucoma Associated with Hypermature Cataract; Phacolytic Glaucoma: A Clinicopathologic Study of 142 Cases
MILTON FLOCKS, STUART C. LITTMAN, and LORENZ E. ZIMMERMAN, San Francisco
Discussion to be opened by S. RODMAN IRVINE, Beverly Hills, Calif.

Evaluation of Metacortandralone and Metacortandracin in Ocular Inflammatory Disease
JOHN H. KING JR. and JOHN B. WEIMER, Washington, D. C.
Discussion to be opened by DAN M. GORDON, New York

Wednesday, June 8

Therapy of Congenital Glaucoma
E. NORRIS ROBERTSON, Oklahoma City
Discussion to be opened by JOSEPH S. HAAS, Chicago

Report on Thirteen Eyes with Congenital Glaucoma Treated by Goniopuncture
GEORGE S. TYNER and EDWARD J. SWETS, Denver
Discussion to be opened by JOSEPH S. HAAS, Chicago

Mechanical Changes During Accommodation Observed by Gonioscopy
HERMANN M. BURIAN, Iowa City
Discussion to be opened by ARTHUR LINKSZ, New York

Treatment of Monocular Cataracts
EVERETT L. GOAR, Houston, Texas
Discussion to be opened by JOHN M. MCLEAN, New York

Ocular Significance of Intracranial Calcium Deposits
JOSEPH E. ALFANO and HARVEY WHITE, Chicago
Discussion to be opened by FRANK B. WALSH, Baltimore

Conjunctivitis Associated with Adenoidal-Pharyngeal-Conjunctival Virus Disease
RALPH W. RYAN, JAMES F. O'ROURKE, GILBERT ISER, ROBERT J. HUEBNER, JOSEPH A. BELL, and ROBERT H. PARROTT, Bethesda, Md.
Discussion to be opened by ALSON E. BRALEY, Iowa City

Thursday Morning—June 9

Address of Invited Foreign Guest
JAMES H. DOGGART, London, England

A New Ptosis Operation Utilizing Both Levator and Frontalis
ROBERT A. SCHIMEK, Detroit
Discussion to be opened by R. N. BERKE, Hackensack, N. J.

Experimental Studies on a New Method of Temporary Shortening of the Inner Coats of the Eye
ANGELOS DELLAPORTA, Buffalo
Discussion to be opened by DOHRMANN K. PISCHEL, San Francisco

Cataract Surgery in Megalocornea: A Case Report of Two Extractions and Review of Cases Since 1931
JOHN W. SMILLIE, Ann Arbor, Mich.
Discussion to be opened by DERRICK VAIL, Chicago

Electromyography of the Extraocular Muscles
GOODWIN M. BREININ and JOSEPH MOLDAVER, New York
Discussion to be opened by FRANCIS H. ADLER, Philadelphia

Treatment of Chronic Glaucoma with Administration of Acetazoleamide (Diamox)
BERNARD BECKER, St. Louis
Discussion to be opened by ROBERT R. TROTTER, Boston

Diamox in Treatment of Flat Postoperative Anterior Chamber Following Glaucoma Surgery
HARVEY E. THORPE, Pittsburgh
Discussion to be opened by PAUL C. CRAIG, Reading, Pa.

Flat Anterior Chambers
JOHN BELLOWS, HOWARD LIEBERMAN, and IRA ABRAMSON, Chicago
Discussion to be opened by PETER C. KRONFELD, Chicago

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY

Tuesday, June 7—1 p. m.

St. Dennis Room, Dennis Hotel

1:00: **A New Interpretation of the Fundus Reflexes**
ARTHUR J. BEDELL

1:20: **Goniocycloscopy and Ophthalmoscopy with the Allen-Thorpe Gonioprism**
HARVEY E. THORPE

1:40: **Biochemistry of Visual Excitation**
GEORGE WALD

2:40: **Intermission**

2:50: **Studies in the Photopic-Scotopic Relationships in the Human Electroretinogram**
EDGAR AUERBACH and HERMANN M. BURIAN

3:10: **Metabolic Injuries of the Visual Cell**
WERNER K. NOELL

3:30: **Electroretinographic Changes Following Administration of Neotetrazolium, Dithizone, and Alloxan to Animals**
ROBERT J. DAVIS and G. PETER ARNOTT

3:50: **Studies on the Visual Toxicity of Methanol: Additional Observations on Methanol Poisoning in the Primate Test Object**
ALBERT M. POTTS, JULIUS PRAGLIN, IRENE FARKAS, L. ORBINSON, and DONALD CHICKERING

4:10: **Retinal Changes Following Ionizing Radiation**
P. A. Cibis and D. V. L. Brown

4:30: **Astroglia in the Human Retina**
J. Reimer Wolter

Wednesday, June 8—1 p. m.

St. Dennis Room, Dennis Hotel

1:00: **A Reversible Hydration and Cation Shift of the Cornea**
John E. Harris and Loretta T. Nordquist

1:20: **Some Biochemical Characteristics of Acid Injury of the Cornea: 1. Ascorbic Acid Studies**
M. A. Guidry, J. H. Allen, and J. B. Kelly

1:40: **Lens-Induced Endophthalmitis: III. Experimentally Produced Bilateral Endophthalmitis Phacoanaphylactica**
Wood Lyda and Stuart W. Lippincott

2:00: **Business Meeting**

2:20: **Intermission**

2:30: **Symposium: Recent Trends in Diamox Research,** V. Everett Kinsey, Presiding

Effect of Diamox upon Composition of the Rabbit Aqueous Humor
Bernard Becker

Mechanism of Action of Diamox and Formation of Aqueous Humor
Harry Green and Irving H. Leopold

Further Studies on Diamox and Aqueous Flow Jonas Friedenwald

Diamox and Intraocular Fluid Dynamics V. Everett Kinsey, Enriqueta Camacho, Gerard Cavanaugh, Marguerite Constant, and Daniel A. McGinty

Carbonic Anhydrase Activity and the Distribution of Diamox in the Rabbit Eye E. J. Ballintine and T. H. Maren

Thursday, June 9—1 p. m.

St. Dennis Room, Dennis Hotel

1:00: **Effect of Sympathetic Nerve Stimulation on the Ciliary Muscle**
G. A. Brecker, C. E. Melton, and Edward W. Purnell

1:20: **Spontaneous and Radiation-Induced Iris Atrophy in Mice**
W. H. Benedict, K. W. Christenberry, and A. C. Upton

1:40: **Effect of Beta Irradiation on Ocular Wound Healing**
James E. McDonald and Howard Wilder

2:00: **Tissue Culture Methods Used in Isolation of the Unknown Group of Eye Viruses**
Ann Fowle, Anne Cockeram, and H. L. Ormsby

2:20: **Tissue Culture Techniques in the Study of Herpetic Infections of the Eye**
Frances W. Doane, A. J. Rhodes, and H. L. Ormsby

2:40: **Studies of Immunity in Vaccinia Keratitis in Rabbits**
J. S. Speakman and H. L. Ormsby

3:00: **Observations on the Effect of the Corticosteroid Hormones on Clinical and Experimental Herpetic Keratitis**
Samuel J. Kimura and Phillips Thygeson

3:20: **Intermission**

3:30: **Penetration of Cortisone and Hydrocortisone into the Ocular Structures**
S. Hamashigi and Albert M. Potts

3:50: **Mitotic Activity in Epithelia of Cultured Lenses**
V. Everett Kinsey, Carl Wachtl, Marguerite Constant, and Enriqueta Camacho

4:10: **Ascorbic-Dehydroascorbic Acid as an Oxidation-Reduction System in the Maintenance of the Metabolism of Lens Cultured in Vitro**
Bernard Schwartz and P. J. Leinfelder

4:30: **Anaerobic Carbohydrate Metabolism of the Crystalline Lens: Generation of High-Energy Phosphate**
Harry Green, Carol A. Bocher, and Irving H. Leopold

GENERAL NEWS

Ophthalmologists of the Americas to Meet in Santiago, Chile, in 1956.—Ophthalmologists of the Western Hemisphere will assemble for the Fifth Pan-American Congress of Ophthalmology in Santiago, Chile, Jan. 9 to 14, 1956, under the presidency of Dr. Moacyr E. Alvaro, of São Paulo, Brazil.

Thirty or more eye specialists from the United States will take part in the program, which is to include symposiums on the following topics: glaucoma, collagen diseases, strabismus, detachment of the retina, tumors of the eye, plastic surgery, physiopathology and surgery of the crystalline lens, tropical diseases affecting the eye, psychosomatic diseases, visual fields, and neuro-ophthalmology.

Moderators for the symposiums, which will have from 4 to 10 speakers each, will include the following from the United States: Drs. John McLean and Algernon B. Reese, New York; Peter Kronfeld, Daniel Snydacker, and Derrick Vail, Chicago, and A. Edward Maumenee, San Francisco. Those from other countries of the hemisphere will be Drs. Jorge Valdeavellano, Lima, Peru; Feliciano Palomino Dena, México D. F., Mexico; Humberto Escapini, San Salvador, El Salvador; Juan Verdaguer and Alberto Gormaz, Santiago, Chile; Durval Prado, São Paulo, Brazil; A. Magin Diez, Manuel Oribe, and Esteban Adrogue, Buenos Aires, Argentina.

The Pan-American Association of Ophthalmology, which was founded in 1939, now has some 1500 members, representing all the 22 countries of the western half of the world. Its first Congress was held in Cleveland in 1940, under the sponsorship of the American Academy of Ophthalmology and Otolaryngology. The succeeding Congresses convened in Montevideo, Uruguay, in 1945; Habana, Cuba, in 1948, and México, D. F., Mexico, in 1952. As interest grew rapidly in the new organization, it was decided that interim meetings would be advantageous. The first of these took place in Miami Beach, Fla., in 1950, in cooperation with the National Association for the Prevention of Blindness (U. S.). The second was held on a Caribbean cruise in January, 1953, with scientific sessions on shipboard and at various ports of call with local groups of ophthalmologists. The third interim meeting was in São Paulo in June, 1954, as an official event of the celebration of the 400th anniversary of the founding of the city.

Each member country of the Association is represented by one vice-president, except the United States, which has two—Drs. William L. Benedict, Rochester, Minn., and Derrick Vail, Chicago. There are two secretaries: For countries north of Panama, Dr. Thomas D. Allen, Chicago (Dr. Daniel Snydacker, 109 N. Wabash Ave., Chicago, is acting secretary at present), and for countries south of Panama, Dr. Jorge Balza, Buenos Aires. There are also assistant secretaries, among whom are the following for the United States: Drs. James H. Allen, New Orleans; Franklin M. Foote, New York; John L. Matthews, San Antonio, Texas; A. Edward Maumenee, San Francisco; Edward McKay, Amarillo, Texas; J. Wesley McKinney, Memphis, and Brittain F. Payne, New York.

PERSONAL NEWS

Dr. Edgar B. Burchell Dinner.—A subscription dinner honoring Edgar B. Burchell, D. Sc., on the completion of 60 years of distinguished service at the New York Eye and Ear Infirmary, will be given on Friday, June 10, 1955, at the 7th Regiment Mess, 643 Park Ave., at 67th St., New York: Cocktails and reception at 6:30 p. m. and dinner at 7:30 p. m. For further information write Dr. Joseph H. Krug, secretary-treasurer, Alumni Association, New York Eye and Ear Infirmary, 218 Second Ave. New York.

Books

Principles of Internal Medicine. Second edition. Edited by T. R. Harrison, Raymond D. Adams, Paul B. Beeson, William H. Resnick, George W. Thorne, and M. M. Wintrobe. Price, $16.00 (1 Vol.); $21.00 (2 Vols.). Pp. 1,703, with index. The Blakiston Company, Inc., 575 Madison Ave., New York 22, 1954.

This textbook of general medicine is edited by a board of outstanding internists, with a large group of contributors from all over the country. There are no chapters dealing directly with the eye, but it is a good reference book for general medical information, brought up to date.

Anthropological and Ophthalmological Studies on the Angmagssalik Eskimos. By Erik Skeller. Price, not given. Pp. 231, with 21 figures; 86 tables. Bianco Lunos Bogtrykkeri A/S, Copenhagen, 1954.

With the development of the air base at Thule, a group of approximately 300 polar Eskimos have been brought into contact with civilization, an association which previously had been totally denied them because of the difficulties of travel. It was the aim of this study to record as many observations as possible from this population before contact with the outside world changed them. While this monograph deals with observations and measurements on the general anatomy of the Eskimo, special interest has been devoted to the ophthalmological sections, which deal with the measurements of the exterior of the eye and with refraction. Up until now, information concerning the Eskimo has been almost completely lacking. This study will be of value to those whose ophthalmological interests cross those of the anthropologist.

Geriatric Medicine. Edition 3. By J. Stieglitz, with 48 contributors. Price, $15.00. Pp. 718, with 205 illustrations. J. B. Lippincott Company, E. Washington Sq., Philadelphia 5, 1954.

Since a large proportion of the patients with which an ophthalmologist has to deal are aging, if not aged, it is important that he be kept abreast of the problems peculiar to old age, and their solution by the newly organized science, geriatrics. This book, first published in 1943, has been one of the standard texts of gerontology, which is the science of aging in its broadest sense. In the generalized field it has a well-deserved reputation, and this third edition testifies to its popularity. The section on Diseases of the Eye has been contributed by Dr. Benjamin Rones, who among the 48 contributors is the sole ophthalmologist. It seems unfortunate that he has been allotted only six and a half pages in which to depict the eye changes, physiologic and pathologic, which are peculiar to growing old, especially since failing vision is such a frequent accompaniment of senility and one of the hardest crosses to bear, coming as it does when other interests and activities are denied the individual.

In the section on diabetes, likewise, this reviewer was considerably disturbed to find so little mention of visual impairment from diabetic retinopathy. Even under the section on complications no mention is made of ocular disabilities, nor is there any discussion of the relative merits of controlled vs. uncontrolled diets in the prognosis as far as retinopathy is concerned. The word retinopathy does not even appear in the index. The inevitable conclusion is that ophthalmologist may become better acquainted with the general physical ills of his patients through this book, but that it forms a very poor text for the general practitioner in acquainting him with the manifold ways in which the declining years of his patients may be made miserable by failing sight. It is to be hoped that this oversight will be remedied in future editions.

Human Physiology. Second Edition. By Bernardo Hussay. Price, $12.50. Pp. 1177, with 504 illustrations. McGraw-Hill Book Company, 330 W. 42d St., New York 36, 1955.

The second edition of this valuable text on physiology contains an excellent section on the physiology of the eye. Three chapters, totaling 47 pages, are devoted to a concise and up-to-date report of the functions of the eye as an optical instrument and a sense organ. The section on visual pigments and their breakdown by light and resynthesis is especially well done, incorporating quite recent work of Wald on the chemical cycle of rhodopsin. The formation of aqueous humor and the maintenance of the intraocular pressure should be revised in a future edition.

This is an excellent text to use as an introduction to the physiology of the eye or as a review for examination purposes.

Human Physiology. By W. B. Youmans, M.D. Price, $6.00. Pp. 481, including glossary and index, with 226 illustrations. The Macmillan Company, 60 Fifth Ave., New York 11, 1954.

This short text of human physiology cannot be recommended as an introduction for students to the physiology of the eye. The materials, in particular, the formation of aqueous humor and the maintenance of intraocular pressure, has not been brought up to date. The section on the pupil and the neuropathways for vision are adequate, but in future editions this whole chapter should be revised. The rest of the book is beyond the interest of this review.

Viral and Rickettsial Diseases of the Skin, Eye and Mucous Membrane of Man. Harvey Blank, M.D., and Geoffrey Blake, M.B., B.S. Price, $8.50. Pp. 285, including index, with 62 illustrations and 7 color plates. Little, Brown & Company, 34 Beacon St., Boston 6, 1954.

This book contains a great deal of information of value to ophthalmologists, although it is not written either by an ophthalmologist or primarily for those specializing in diseases of the eye. There is a good introduction on the nature of viruses and rickettsia, together with a chapter on the general diagnosis of the diseases caused by these pathogens. The various diseases caused by viral and rickettsial agents are then considered, such as herpes, chickenpox and zoster, smallpox and vaccinia, the exanthematous diseases, the common cold, herpangina, warts, molluscum contagiosum, viral diseases contracted from animals, epidemic keratoconjunctivitis, the Chlamydozoaceae, and, finally, the rickettsial diseases.

The book is beautifully illustrated, and is an authoritative text on the material it covers.

Codigo de la ceguera. By Dr. Tomás R. Yanes. Price, not given. Pp. 264; with 2 illustrations. Editorial Echevarría, Fomento No. 114, Luyano, Habana, Cuba, 1954.

This paper-bound volume was prepared by the author for the League Against Blindness of the Republic of Cuba to urge the formation of a National Corporation of Blindness and to propose laws for this purpose. The first three chapters deal with the problem of blindness in the Americas, a survey of blindness in Cuba, and a review of the psychological factors relating to blind persons. The next chapters are concerned with social assistance, education, and occupations for the blind, and a section on the history of canes and guide dogs used by the blind. The author then discusses the problem as it is being met in the countries of North and South America and Spain, and the development of organizations for the prevention of blindness. The final chapter contains the proposals for legislation, followed by a bibliography.

Neuro-Ophthalmology. Edition 2. By Donald Lyle, M.D. Price, $17.50. Pp. 591, including index, with 335 illustrations. Charles C Thomas, Publisher, 301 E. Lawrence Ave., Springfield, Ill., 1954.

In the second edition of this popular text on neuro-ophthalmology the author has amplified the sections dealing with basic anatomy and physiology. Of the first four chapters dealing with the visual system, the first seventeen pages are devoted to anatomical and physiological considerations. The essential virtues of the first edition have been retained, however. In this reviewer's opinion, the emphasis on correlation of the clinical symptoms with postmortem or operative findings has been the chief contribution this text has made. The beautiful anatomical drawings with fiber tracts filled in diagrammatically add much to the value of the book as a source of teaching. It would be hard to picture a better method of describing various syndromes, such as the Foster-Kennedy syndrome, the meningioma syndrome, etc., than has been done graphically in Chapter 24. The arrangement of material has been somewhat loose—the first fourteen chapters on an anatomical basis and the remaining nine on a disease classification.

The only criticism which might be made would be the suggestion that in the next edition the author considerably enlarge the index, which is hardly adequate if the book is to be used as a teaching text.

Hand Atlas and Textbook of Human Anatomy. Two Volumes. Werner Spalteholtz. Fifteenth Edition, revised and enlarged by Rudolf Spanner. Price, each volume, $11.50. Vol. II: Vascular System, Viscera, Nervous System, Sense Organs. Pp. 454, with 776 plates. Little, Brown & Company, 34 Beacon St., Boston 6, 1955.

This famous Atlas has gone through 15 editions and still retains its individuality and excellence. Part II is of special interest to ophthalmologists because of the section on the central nervous system and the section on the eye. The section on the eye contains 43 plates, all of which are beautifully executed. The material includes some of the recent work on the canal of Schlemm and the lamina choriocapillaris by means of neoprene casts, done by Ashton.

Two Lectures on Biomicroscopy of the Eye. By Dr. Hans Goldmann. Price, not given. Pp. 55 with 63 illustrations. Rosch, Vogt & Co., Berne, Switzerland, 1954.

The two lectures included in this booklet were delivered in 1933 before the Brazilian Ophthalmological Society and the University of São Paulo in Rio de Janiero and São Paulo, and at the University of Iowa on the occasion of the Symposium on "Problems in Physiology and Pathology of the Eye" in September, 1954.

The first lecture is entitled "An Introduction to Gonioscopy." The anatomical relationships of the angle are reviewed, and the author acquaints those of us who have not used his particular mirror contact glass with this simple device. Various clinical entities are then described, from aniridia to injuries and retained foreign bodies, in all of which the gonioscopic appearance of the angle is of great clinical value. Obviously, the section on glaucoma is the most important.

The second lecture is entitled "The Examination of the Vitreous and the Fundus with the Slitlamp." The author prefers the use of a contact glass after maximum mydriasis is achieved, with a reducing prism which enables the angle between the eliminating device and the microscope to be small when examining the fundus and large when the vitreous is the object of scrutiny. Numerous entities are described, among the more important of which are detachment of the vitreous, the changes which occur in the periphery of the retina in retinal detachment, and various conditions of the optic disc and the macula.

Both these lectures are abundantly illustrated with beautiful drawings, and great credit must be given Mr. Iseli and Miss Meyer by the readers of this book, as the author himself has done, for they enhance the value of it greatly. Anything

from the pen of this genial and brilliant investigator and clinician is a welcome addition to our literature. It is to be hoped that more of these will follow. These two lectures were made possible by the generosity of Messrs. Haag-Streit, of Berne, Switzerland.

Education and Health of the Partially Seeing Child. Third Edition. By Winifred Hathaway. Price not given. Pp. 227, including index, with 11 figures. Columbia University Press, 2960 Broadway, New York 27, 1954.

Every ophthalmologist should know something of the history of the special educational facilities for visually handicapped children. This book gives an excellent historical background, and defines the needs of the partially seeing child in respect to special educational facilities and the methods of providing these. In addition to its usefulness as part of the general education for every ophthalmologist, this book will be of interest to administrators, supervisors, teachers, nurses, social workers, and all others concerned with the welfare of the visually handicapped child. An adequate appendix gives a glossary of terms and general instruction about the eye to lay readers.

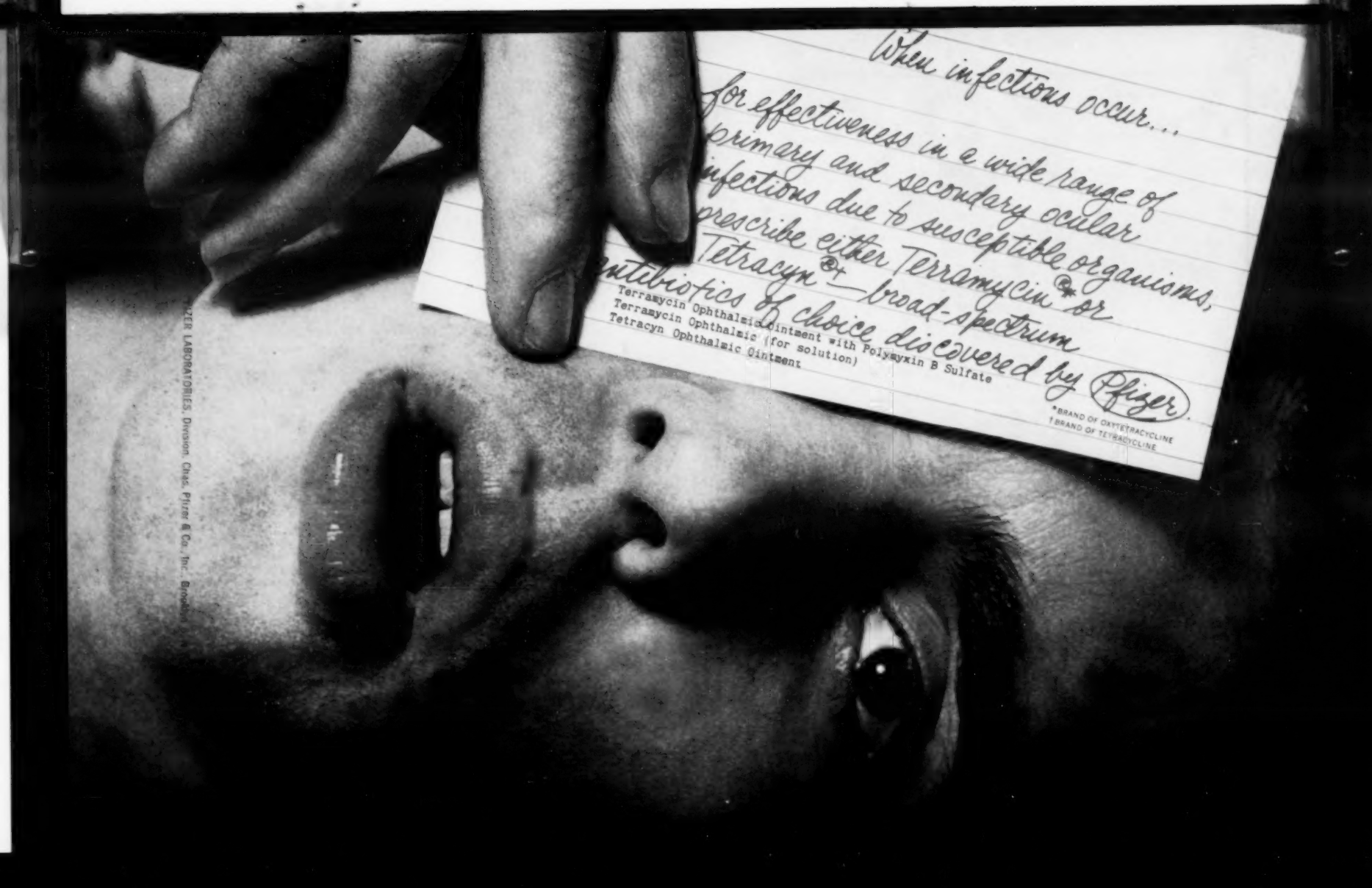
Cytoarchitecture of the Human Brain Stem. Jerzy Olszewski and Donald Baxter. Price, $16.00. Pp. 199, with 170 illustrations. J. B. Lippincott Company, 227-231 S. 6th St., Philadelphia 5, 1954.

This atlas of the brain stem brings up to date anatomical investigation primarily concerned with patterns of arrangement and morphological details of nerve cells as revealed by magnifications within the range of the ordinary microscope (cyto-architectonics).

The first part of the monograph consists of a series of nineteen semischematic representative cross sections of the brain stem, accompanied by low-power photomicrographs. Descriptions of the individual nuclei, supplemented by photomicrographs of higher magnifications, compose the second part.

This atlas will prove of value to the neuroanatomist who is interested in the position and morphology of the individual nuclei and to the neuropathologist in his attempts to localize pathological processes and to distinguish abnormal from normal cell forms found within various regions of the brain stem. The neurophysiologist may find it useful to have available detailed human morphological data which can be correlated with those on experimental animals and with which his functional concepts may be integrated.

The book is of interest to ophthalmologists only in so far as they are interested in neuro-ophthalmology and correlated studies, as cited above. It does belong in libraries alongside the classic atlases of the nervous system.


When infections occur...
for effectiveness in a wide range of
primary and secondary ocular
infections due to susceptible organisms,
prescribe either Terramycin® or
Tetracyn†—broad-spectrum
antibiotics of choice discovered by Pfizer.
Terramycin Ophthalmic Ointment with Polymyxin B Sulfate
Terramycin Ophthalmic (for solution)
Tetracyn Ophthalmic Ointment
*BRAND OF OXYTETRACYCLINE
†BRAND OF TETRACYCLINE
ZER LABORATORIES, Division, Chas. Pfizer & Co., Inc., Brooklyn

A necessity in every eye operating room and wherever eye injuries are treated.

OPHTHALMOS

Sterile, fully potent eye medications
in the new

steridroppa
trademark
pat. pend.

Single Dose Disposable Dropper Unit

all important solutions
required for ocular surgery *available in the*

write now for details to OPHTHALMOS, INC.
UNION CITY, N. J.

Do you dispense glasses?

We are one of the oldest, and most reputable wholesale opticians in the east, serving the discriminate ophthalmologist.

An inquiry from you will bring a representative at your convenience to outline our superior service plan.

MAX ZADEK, INC.

established 1904

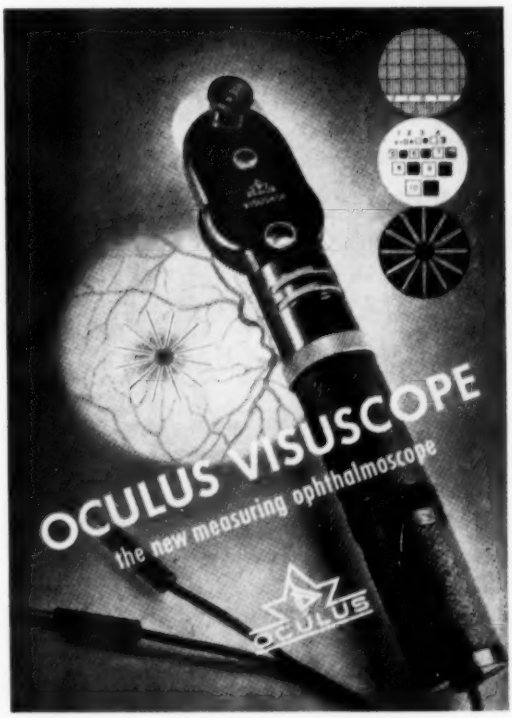
115 Fulton Street New York 38, N. Y.

THE NEW Rodenstock EYE-REFRACTOMETER

Excellent for the objective determination of refractions of the human eye, the Rodenstock eye-refractometer permits instantaneous readings of spherical and cylindrical refractions including inclination of the axis. Enables you to diagnose objectively problem cases like children, illiterates, cases of pin hole pupils, as size of pupil has no effect on efficiency. Eliminates time consuming basic diagnosis so tiring to the patient. Particularly helpful in difficult cases of strong astigmatism and sensitive or nervous patients. This instrument stimulates the patient's confidence in the doctor as well as self-confidence of the patient. Range from plus 20.D to minus 20.D.

THE VISUSCOPE *The Ophthalmoscope PLUS*

- Retinoscopy with erect or inverted image
- Determination of area and position of infectious processes within anterior portion of the eye and fundus
- Measurement of level differences
- Measurement of blood vessel widths
- Objective determination of refractive error, including astigmatism and its main meridians
- Determination of fixation point of retina in cases of monocular excentric fixation
- Eliminates accommodation of examiner due to optical system
- Fingertip control
- Adjustability to patient's refractive error ranging to ± 25.D.
- Automatic switch turns light on or off as instrument is picked up or put down
- Well cooled handle



A 555

ANTON HEILMAN
220 Main St.
Hempstead, L.I., N.Y.

Kindly send the following catalogues

- ☐ RODENSTOCK EYE-REFRACTOMETER
- ☐ RODENSTOCK VERTEX REFRACTIONOMETER
- ☐ RODENSTOCK TEST LENS SETS AND TRIAL FRAMES
- ☐ RODENSTOCK OPHTHALMIC FRAMES
- ☐ KRAHN BINOCULAR OPHTHALMOSCOPE OFE
- ☐ KRAHN OPHTHALMOMETER BE
- ☐ KRAHN PRISM EXOPHTHALMOMETER C
- ☐ KRAHN RAPID CHANGE INSTRUMENT TABLE WEZ
- ☐ KRAHN SCOTOMETER D
- ☐ KRAHN UNIVERSAL REVOLVING OPHTHALMIC UNIT
- ☐ KLEIN'S PHOROMETER
- ☐ SARWAR DIAGNOSTIC CONTACT LENS
- ☐ PERIMETER OF DR. ETIENNE
- ☐ VISUSCOPE — THE NEW MEASURING OPHTHALMOSCOPE
- ☐ OPERATING LOUPES
- ☐ LISTER-MORTON OPHTHALMOSCOPE
- ☐ PURVIS STREAK RETINOSCOPE
- ☐ PROFESSOR AMSLER CHARTS (TO DETECT METAMORPHOPSIA, RELATIVE SCOTOMA)
- ☐ DIPROSE HAND SLIT LAMP 7 FOCAL ILLUMINATOR
- ☐ REXOMETER
- ☐ EYE SURGICAL INSTRUMENTS
- ☐ OPTICAL PLIERS, TOOLS FOR YOUR DISPENSER

NAME .....

ADDRESS .....

CITY .....

STATE .....

E. B. Meyrowitz

SURGICAL INSTRUMENTS CO., INC.,
520 FIFTH AVENUE, NEW YORK 36, N. Y.

LONDON *ESTABLISHED 1875* PARIS

ATKINSON SCLERATOME

Dr. Walter S. Atkinson—Watertown, N.Y.

The Atkinson Scleratome was devised to make the incision for preplaced sutures, as it is often difficult to make a clean incision the proper length and depth with the cutting instruments generally used for this purpose, especially if the eye is soft. In this new instrument the depth of the blade and thickness of the shaft guard against making the cut too deep. This scleratome may also be used to make a scratch or ab externo incision or to outline the sclera to be removed in scleral resections.

Price $6.50 ea.

HERTEL EXOPHTHALMOMETER

Improved over the original German model, in that is has front surface mirrors which do away with parallax, this exophthalmometer enables the examiner to measure the degree of exophthalmos accurately and rapidly without assistance.

The right member slides over a calibrated millimeter rule. Each member has two mirrors mounted at right angles, one above the other. When the instrument is in position, with the two outer points in contact with the temporal margin of each orbit, the profile of the cornea is seen in one mirror and the scale in the other. The scale reading directly above the corneal image gives its protrusion in millimeters.

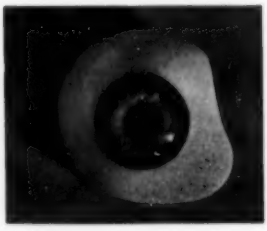
The separation of the two members is shown on the slide. All measurements of the same case must be made with the members separated to the same reading on the sliding scale. Supplied in case.

Price $55.00

Specialists in ALL TYPES of Plastic and Glass Artificial Human Eyes Exclusively

MADE TO ORDER IN OUR OWN LABORATORY

Doctors are invited to visit



REFERRED CASES CAREFULLY ATTENDED AND SATISFACTION GUARANTEED

EYES ALSO FITTED FROM STOCK

Plastic or Glass Selections Sent on Memorandum upon Request

Implants and Plastic Conformers in Stock

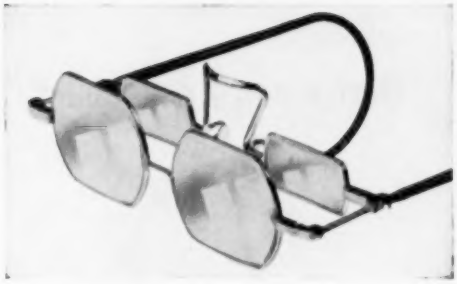
FRIED AND KOHLER, INC.

665 FIFTH AVENUE
near 53rd St.

NEW YORK, N. Y.
Tel. ELdorado 5-1970

MAGNOCULAR

. . . A Perfect Magnifying Spectacle

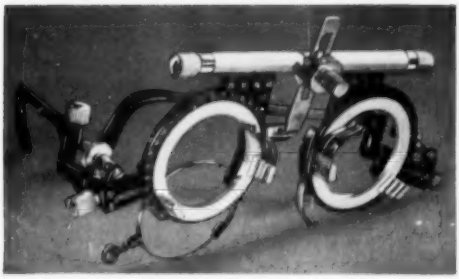


Ophthalmologists thruout the country use this French telescopic loupe for precise operation and examination while both hands are free. Telescopic system guarantees minimum of distortion at 2x magnification. Large flat field at eight inch focal distance. Visual prescription may be incorporated by two methods. Rx model has special empty eye-wire frame. In standard model add Rx to minus power of ocular lenses In either case the visual prescription becomes part of the telescopic system.

For patients: Since the MAGNOCULAR provides an enlarged retinal image which increases the number of nerve receptors used, it is indicated in cases of macular degeneration and, generally, where reading difficulty exists after full correction.

Collapsible feature allows it to be carried in a standard spectacle case. Returnable for credit after full inspection.

for standard model $22.50
$25.00 for Rx model



GRAFFE TRIAL FRAME

• Light duralumin all-metal frame • Simple, precise construction for lifetime service • Enclosed gears. • **An exclusive feature—accessory cells demonstrate to patient exact bifocal lens arrangement** • Exact corneal alignment • Fully adjustable lens holders are automatically locked in any position • Full pantoscopic and retinoscopic temple adjustment—adjustable nose rest—height adjustment and individual P.D. measurement • Extra space allows easy—no fumbling—insertion of lens • Accepts all 1½ inch trial lenses • Returnable for credit after full inspection.

$39.50

ARMCO MERCANTILE COMPANY
221 N. LaSalle St. Chicago 1, Ill.

"Doctor, am I color blind?"

You will give your patients the correct answer if you use the new 2nd Edition of the DVORINE COLOR PLATES.

The DVORINE PSEUDO-ISOCHROMATIC PLATES uncover not only weaknesses in color perception, but in color nomenclature as well.

Here are some of the desirable features which are found ONLY in the DVORINE COLOR PLATES:

- **A test for color nomenclature, to distinguish the color blind from the color ignorant.**
- **A special section for testing very young children and illiterates.**
- **Each plate is limited to two color combinations, making a diagnosis more positive.**
- **The set consists of 23 plates with eight different color combinations, for the identification of specific confusion colors.**
- **A six-ring loose-leaf binder for rapid change of plates sequence, to outwit the malingerer.**

ACCEPTED

MAIL THIS COUPON

Scientific Publishing Co.
Dept. A — **$12.00**
2328 Eutaw Place — **complete set**
Baltimore 17, Md.

Send me a copy of the new
"DVORINE PSEUDO-ISOCHROMATIC PLATES"
(with directions)

Name .....

Address .....

City ..... **Zone** .... **State** .....

☐ **Remittance Enclosed** ☐ **Bill Me.**

If check accompanies order, you may deduct a cash discount of 5%, that is, send only $11.40.

(Money cheerfully refunded if you are not satisfied with the set when you receive it.)

POSTGRADUATE COURSE
and
SUMMER CONVENTION OF THE COLORADO OPHTHALMOLOGICAL SOCIETY
and the
UNIVERSITY OF COLORADO MEDICAL CENTER

Denver, Colorado

July 25, 26, 27, 28, 1955

The program will consist of lectures, seminars and demonstrations of interest to both the specialist and the practitioner caring for Eye Diseases.

Registration will be open to all members of the Society and qualified physicians on a limited membership basis. Tuition $40.00.

Plan now to attend and combine an intensive review of advances in this specialty with your summer vacation.

Complete program and details will be mailed upon request addressed to:

Director of Postgraduate Medical Education
University of Colorado School of Medicine
4200 East Ninth Avenue
Denver 20, Colorado

THE WASHINGTON UNIVERSITY SCHOOL OF MEDICINE

DEPARTMENT OF OPHTHALMOLOGY

announces its

THIRTY-FIFTH ANNUAL 8-MONTH COURSE IN THE BASIC SCIENCES OF OPHTHALMOLOGY

September 19, 1955—May 18, 1956

1-WEEK INTENSIVE COURSE IN PATHOLOGY OF THE EYE AND ADNEXA

September 12-17, 1955

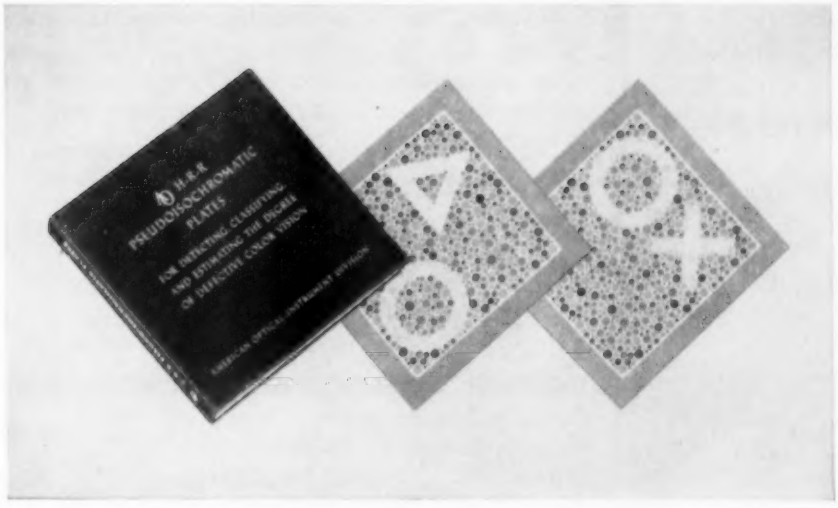
Both courses are limited

For more detailed information write to:

Department of Ophthalmology

Washington University School of Medicine

640 S. Kingshighway Blvd.
St. Louis 10, Missouri



Announcing

The NEW AO H-R-R

PSEUDOISOCHROMATIC PLATES

by LeGrand H. Hardy, M.D.
Gertrude Rand, PH.D.
M. Catherine Rittler, B.A.

Based on the research work originally conducted in the Knapp Memorial Laboratory of Physiological Optics, the Institute of Ophthalmology of Presbyterian Hospital and the Department of Ophthalmology of the College of Physicians and Surgeons of Columbia University, New York, New York.

American Optical announces the most comprehensive low-cost color test ever produced. Many years in development, it has a scope and thoroughness never before achieved in a test of this type. Extremely easy to administer, it makes complete, accurate color vision testing a logical facility of every office.

First, it separates people with defective Red-Green and/or Blue-Yellow color vision from those with normal color vision. Further, it classifies the subject's defect as to Protan, Deutan, Tritan or Tetartan. Finally it estimates the amount of the deficiency as mild, medium or strong.

The development of the test has been so successful that it combines speed and ease of administration with the new features of classification and quantitative diagnosis. For the vast majority of people the test is completed in seconds. The symbols used are universally understood. The ingenious pattern of the plates allows no clues for memorization. It has been approved by the Subcommittee on Color Blindness Studies of the Inter-Society Color Council.

For a first-hand view of this truly remarkable development in the field of physiological optics, call your AO Representative.

American Optical
INSTRUMENT DIVISION BUFFALO 11, N. Y.

when **safety** is important

Precious eyes are safest behind hard resin Armorlite lenses!

These modern, highly durable lenses are made from hardest, die-cast resin with the same meticulous accuracy as glass.

Armorlite offers your patients the following advantages:

- Four times the resistance to swift impacts of case-hardened safety glass.
- Thirty times more scratch-resistance than the best common plastics.*
- Feather light! (Only *half* the weight of glass).
- Four times the resistance of glass to fogging.

**American Standard Safety Code Z26.1-1950, Test 17*

For children, sportsmen, and all those in eye-hazardous occupations,

ARMORLITE IS YOUR BEST PRESCRIPTION

Available through regular sources of supply, or directly from:

ARMORLITE LENS COMPANY, INC.

117 E. Colorado St., Pasadena, Calif.

Literature sent upon request

Instrumentation for

MICRO-GONIOSCOPY and GONIOTOMY

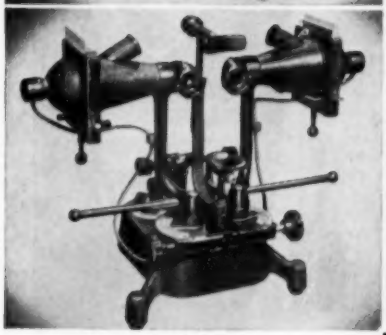
after Otto Barkan, M.D.

Gonioscope

GONIOSCOPE (illustrated) floor model, for office and hospital surgery	$185.00
CORNEAL MICROSCOPE B & L	180.00
CORNEAL MICROSCOPE Haag-Streit	225.00
Your own Corneal Microscope adapted to gonioscope	10.00
Otto Barkan Focal Illuminator (hand lamp) with plug in transformer	42.50
Otto Barkan-Koeppe Diagnostic Lens (for viewing the angle) small (infant) 16 & 17 mm (medium) 18 & 19 large (adult) 20 mm in glass	45.00
Otto Barkan Surgical Goniotomy Lens small (infant) med. (child and adult)	45.00
Otto Barkan Surgical Knife (latest model)	9.75
Otto Barkan Operating Lamp	65.00
Floor stand for above	20.00

PARSONS OPTICAL LABORATORIES, INC.

518–20 Powell Street **San Francisco 2, Calif.**



THE MOORFIELDS SYNOPTOPHORE

from

CLEMENT CLARKE

of

England

The Moorfields Synoptophore has long enjoyed the universal recognition as a most important orthoptic apparatus. Originally evolved from the simple Worth's Amblyoscope, its development has kept pace with the many improvements in orthoptic technique.

When the two optical tubes are moved through any angle the movements are concentric with those of the visual axes. A simple slow motion device is provided for duction exercises, and by releasing a locking key the two tubes may be rotated in co-ordination for kinetic exercises.

Large diameter lenses and stainless steel mirrors, producing a brilliant image, are fitted into eyepieces so shaped to facilitate observation of the corneal reflexes. Auxiliary cells for standard sized trial lenses and prisms are supplied.

The interlenticular distance may be varied from 50 mm. to 80 mm. Interpupillary distances smaller than 50 mm. are perfectly accommodated. Cyclophoria and hyperphoria may be measured with great accuracy and the slow motion vertical screw is also valuable in estimating vertical ductions. Other features include adjustable chin and forehead rests, two flashing switches of the latest micro type and two dimming rheostats.

CLEMENT CLARKE ORTHOPTIC EQUIPMENT INCLUDES:
The Lyle Major Amblyoscope, Hess Screens, Cheiroscopes, Worth's 4 Dot Test, Diplopia Goggles, Rotating E Test, Maddox Handframe, Maddox Wing Test, Bar Readers, etc.

CLEMENT CLARKE of ENGLAND

GUILD OPTICIANS

63, WIGMORE STREET, LONDON, W. 1. ENGLAND

Sole Agents in U.S.A.

CURRY & PAXTON INC., ( ) 101, PARK AVENUE, N.Y. 17. LEXINGTON 2-7842

Today— People go for Comfort—like nothing else!

This is the *Age of Comfort* . . . of casual, loose-fitting apparel, easy footwear, comfortable seating and sleeping, conditioned air — *and* modern, light-weight I-GARD plastic lenses.

This tired-nose gesture is out-of-date!

Undue pressure and strain on the sensitive bridge of the nose is a nagging discomfort *needlessly* suffered by millions of eyeglass wearers now that feather-light I-GARDS are readily available in 90% of prescriptions.

Give your patients light-weight I-GARD comfort

Give them complete freedom from oppressive pressure — better seeing with clearer lenses that are accurate to 1/10,000 of an inch — PLUS shatter-proof safety. They'll tell you, as they tell us, "I couldn't bear to go back to my old eyeglasses."

Send now for I-Gard foci chart, price list, samples and name of nearest I-Gard distributor.

DEPT. E
McLEOD OPTICAL COMPANY, INC.
357 Westminster St., Providence 1, R. I.

i-gard
Plastic Lenses

really Feather-Light

really Non-Shatterable

i-gard

Worn by millions all over the world

TRIAL SETS
(as shown)

$195.00

Includes spheres, cylinders, prism, colored lenses, accessory lenses, 2 trial frames, and P. D. measuring device (other sets to $550.00).

BURTON LAMPS

For examination of corneal lesions, abrasions, and ulceration . . . contact lens fitting . . . removal of foreign bodies . . . examination of lenticular conditions. *Models from $13.50 up.*

Above model $30.00.
With U.V. Bulbs All prices F.O.B. Los Angeles

R. G. BURTON & CO.
MANUFACTURERS & DISTRIBUTORS
2012 Bagley Ave. Los Angeles 34, California

The Berman Metal Locator

An electromagnetic detecting device that quickly and accurately locates metallic foreign bodies, including magnetic intraocular foreign bodies. Metallic fragments are readily detected from a satisfactory distance through intervening bone, tissue and fluids. Probing or physical contact with the foreign body is not required for detection.

The thin sterilizable probe provides preoperative localization, "pin-point" accuracy within the incision and postoperative check.

Lends precision to foreign body surgery and greatly reduces surgical trauma.

BERMAN LABORATORIES
112-03 Rockaway Blvd. Ozone Park 20, N. Y.

Often Preferred

in ophthalmologic practice

ISO-SOL®

STERILE OPHTHALMIC SOLUTIONS

- physiologically active
- exceptionally well tolerated
- buffered for stability
- sterile and bacteriostatic

each dropper bottle is

- sterile
- tamperproof - sealed
- and dated

Atropine Sulf. ½%, 1%, 2%, 4% For dependable mydriasis and cycloplegia.

Eserine Sal. ⅛%, ¼%, ½% notably effective well tolerated isosmotic.

Homatropine HBr. 2%, 5% promptly effective mydriatic isotonic with tears—virtual freedom from side effects.

Pilocarpine HCl. ½%, 1%, 2%, 4% effective direct acting non-allergenic buffered.

The ISO-SOL Co., Inc., Brooklyn 17, N.Y.
Distributors: Montreal, Panama City

ISO-SOL®

Write for a descriptive list of all ISO-SOL products.

ALL PLASTIC

ARTIFICIAL EYES

Individually Created

DAVID A. GROSSBERG INC.
133 EAST 58th STREET NEW YORK 22, N. Y
WICKERSHAM MEDICAL BLDG.

ATTRACTS NEW ALLOY STEELS THAT SMALL MAGNETS DO NOT MOVE

The New Improved Mueller

GIANT EYE MAGNET

Adjustable in Height, Direction and Tilt

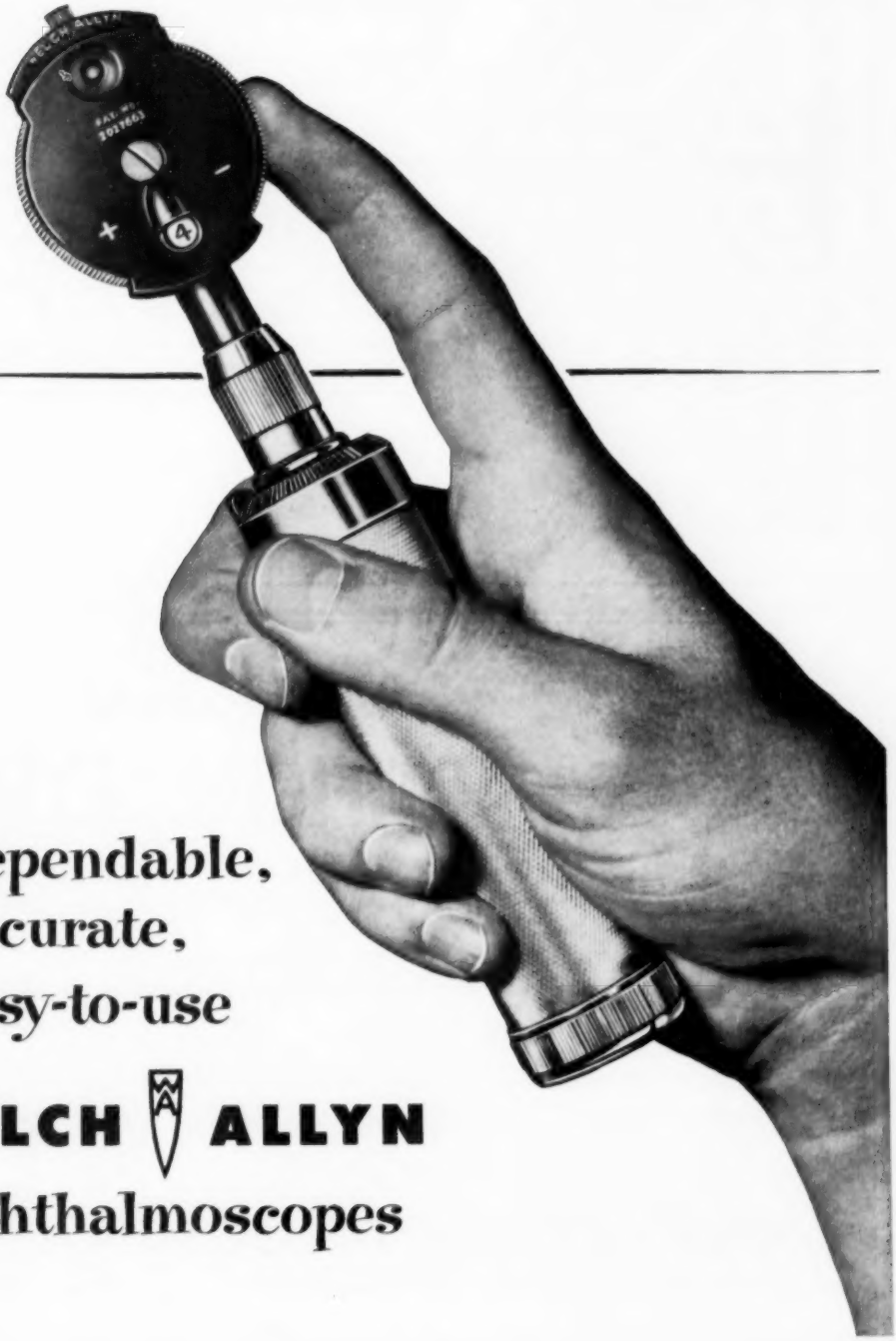
Now equipped with a spark-free, noiseless selenium rectifier and explosion-proof foot-switch control, the Mueller Giant Magnet is better—safer—surer than ever—essential equipment for the modern hospital, clinic, industrial first aid room. Greater power than any comparable magnet provides a much increased range of usefulness, particularly in removal of bits of the newer alloys which are not affected by smaller magnets. Perfectly counterbalanced, the magnet is quickly and silently adjustable in height, direction and tilt—as easy to operate as it is free from maintenance costs. On noiseless casters, complete with interchangeable blunt and probe pointed silvered tips. Early delivery. Write for details.

V. Mueller & Co.

330 SOUTH HONORE STREET
CHICAGO 12, ILLINOIS

BRANCHES NOW IN ROCHESTER (MINN.) — DALLAS AND HOUSTON, TEXAS

Partner in your practice



Dependable,
accurate,
easy-to-use

WELCH ALLYN
Ophthalmoscopes

Rx
QUALITY SERVICE
Technical skills and services that will never let you down
DOW

CONFIDENCE...

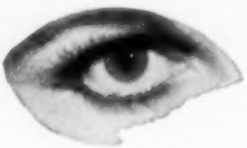
Professional reputations are built on confidence. Your learning and skill and judgment would be fruitless unless you strove to achieve faith on the part of your patients. And even when you have won this trust all your effort is at the mercy of those who interpret your prescriptions.

¶Here at Dow we pride ourselves on the impeccable quality of our eye-wear, which results inevitably from our scrupulous selection of only top-grade materials . . . from the care with which we grind and polish and edge our lenses . . . from our expert placement of them before the eyes in the very best of mountings. All this and more we do . . . that your patients may have fullest confidence in you.

DOW OPTICAL CO.

W. E. DOW, Pres.

Chicago, Ill. Bloomington, Ill.



Most Natural
ARTIFICIAL EYES

Dispensers and makers of fine eyes of plastic and glass. Eyes to fit all types of implants.

Selections sent on memorandum from the most complete group of eyes. Careful attention given to all referred cases.

The Doctor and his patient must be completely satisfied or there is absolutely no obligation.

Of Service Since 1906

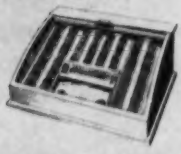
DENVER OPTIC COMPANY

310 University Bldg. Telephone Main 3-5638 Denver 2, Colorado

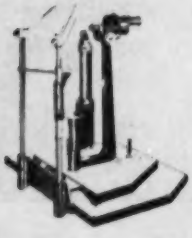
AIMARK PROJECTION PERIMETER

HAND SLIT LAMP

DIAGNOSTIC SET



ROLLERTOP TRIAL CASE & TEST LENSES



AIMARK SLIT LAMP

From its distinguished list of British Optical instruments . . .

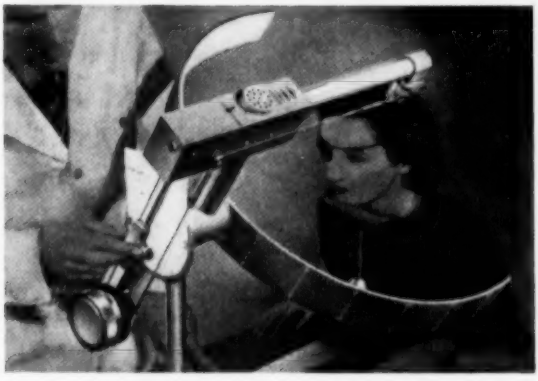
CURRY & PAXTON

LIMITED

of London, England

present the

AIMARK PROJECTION PERIMETER



$720 Developed by the Royal Air Force during World War II from the design of Prof. Maggiore. The Aimark Projection Perimeter presents a test stimulus which is under control as to size, brightness and colour in all parts of the field. It is capable of smooth and silent movement by means of a mechanism demanding minimum attention on the doctor's part. It is a precise means of detecting the position and intensity of lesions in the visual pathway. An additional feature is automatic recording.

Write for brochure AO-5 and further information on this and any other optical instruments listed

FOR YOUR PROTECTION AND CONVENIENCE

Complete service, repair and parts department in our New York workshops

CURRY & PAXTON INC.

Our new address:

230 PARK AVENUE • NEW YORK 17, N. Y.

Manufacturers' Representatives in the U. S. A.

DISTRIBUTORS

Chicago: House of Vision

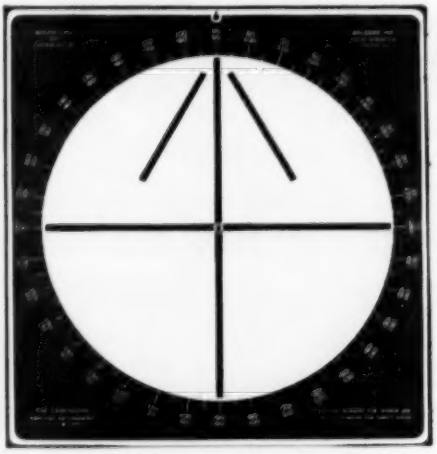
Los Angeles: Spratt Optical • Superior Optical

San Francisco: Parsons Laboratories

Pittsburgh: Doig Optical

MADDOX HAND FRAME

MADDOX WING TEST



(Actual size 13½" x 14")

SIMPLIFIED ASTIGMOMETER

(Lebensohn)

PLASTIC

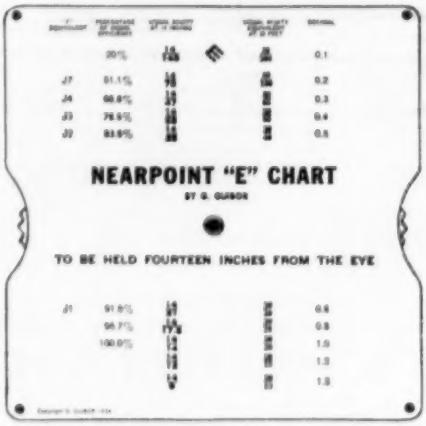
WASHABLE

"NO COMPUTATION REQUIRED"

CAN BE USED AT 10 OR 20 FEET

Send for Literature

EACH $9.75



Actual size 6" x 6"

New Near Chart

GUIBOR Symbol Near Chart now available in durable and soilproof plastic. Gives distance equivalents, as well as quantitative measurements for near vision. E Symbol understood by all.

Place your order now.

$3.25

DISPENSING SERVICE

Loop Office:
109 N. Wabash, at Washington
9th Floor STate 2-5362
CHICAGO, ILL.

Austin Belgard INC.
(Formerly Belgard, Inc.)

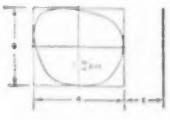
OPHTHALMIC OPTICIANS
WHOLESALE & SERVICE

Wilmette Office:
1139 Central Avenue
WILMETTE, ILL.

IN STEP WITH SPRING . . .

Art-Rim with Spray Trim . .

SPRAY in either white or yellow 1/10-12K Gold Filled makes a beautiful accent on any frame to which it is applied. It is unusually pleasing on Art-Rim Leading Lady. It's delicate tracery masses in color to give perfect balance with the bridge area. Remember to ask your supplier about this new Spray trim.



7m DIFF.

Eye	A	B	E bridge
40	41.5	34.5	18 20 22
42	43.5	36.5	18 20 22 24
44	45.5	38.5	18 20 22 24
46	47.5	40.5	18 20 22 24

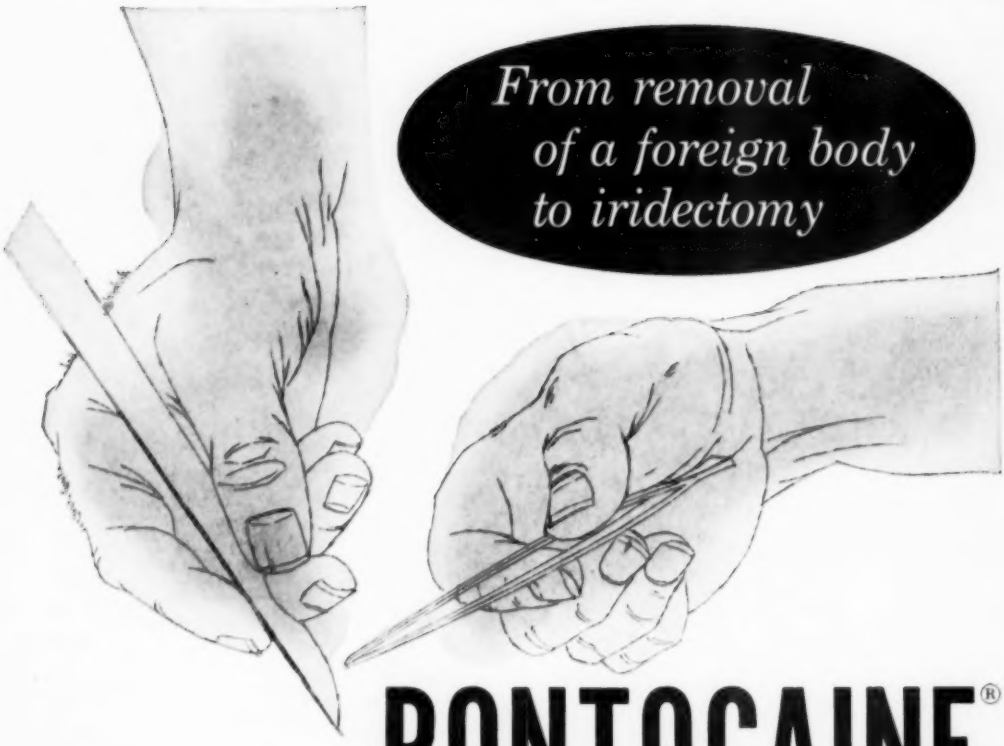
P.D. = A + E 43.5 + 20 = 63.5 P.D.

All colors made to order.

Branch Offices:
NEW YORK • CHICAGO
PHILADELPHIA • LOS ANGELES
CINCINNATI • DALLAS

• MANUFACTURER •

ART-CRAFT
OPTICAL COMPANY
Inc.
ROCHESTER N. Y.



From removal of a foreign body to iridectomy

PONTOCAINE®

HYDROCHLORIDE

—DEPENDABLE, PROLONGED SURFACE ANESTHESIA FOR OPHTHALMIC PROCEDURES

A variety of operative and non-operative procedures on the eye may be successfully carried out with small quantities of 0.5 per cent solution of Pontocaine—

- removal of foreign bodies
- dilatation of tear duct
- tonometry, ignipuncture
- subconjunctival injection of salt solutions
- treatment of conjunctivitis
- iridectomy

Pontocaine is less likely than cocaine to affect the corneal epithelium. Rarely dilates the pupil. Produces no increase in intra-ocular pressure.

Supplied: 0.5% solution, bottles of ½ oz. and 2 oz.

Pontocaine Eye Ointment

for prolonged relief of pain
0.5%, tubes of ⅛ oz.

Winthrop-Stearns INC.
NEW YORK 18, N. Y. WINDSOR, ONT.

Pontocaine, trademark reg. U.S. Pat. Off., brand of tetracaine

Visit our Booths #B 12-14 and C 11-13 A. M. A. Convention, June 6-10, 1955.